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 NEWS  4  Feb 16   TOXLINE no longer being updated
 NEWS  5  Apr 23   Search Derwent WPINDEX by chemical structure
 NEWS  6  Apr 23   PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
 NEWS  7  May 07   DGENE Reload
 NEWS  8  Jun 20   Published patent applications (A1) are now in USPATFULL
 NEWS  9  JUL 13   New SDI alert frequency now available in Derwent's
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 NEWS 10  Aug 23   In-process records and more frequent updates now in
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 NEWS 11  Aug 23   PAGE IMAGES FOR 1947-1966 RECORDS IN CAPLUS AND CA
 NEWS 12  Aug 23   Adis Newsletters (ADISNEWS) now available on STN
 NEWS 13  Sep 17   IMSworld Pharmaceutical Company Directory name change
                   to PHARMASEARCH
 NEWS 14  Oct 09   Korean abstracts now included in Derwent World Patents
                   Index
 NEWS 15  Oct 09   Number of Derwent World Patents Index updates increased
 NEWS 16  Oct 15   Calculated properties now in the REGISTRY/ZREGISTRY File
 NEWS 17  Oct 22   Over 1 million reactions added to CASREACT
 NEWS 18  Oct 22   DGENE GETSIM has been improved
 NEWS 19  Oct 29   AAASD no longer available
 NEWS 20  Nov 19   New Search Capabilities  USPATFULL and USPAT2
 NEWS 21  Nov 19   TOXCENTER(SM) - new toxicology file now available on STN
 NEWS 22  Nov 29   COPPERLIT now available on STN
 NEWS 23  Nov 29   DWPI revisions to NTIS and US Provisional Numbers
 NEWS 24  Nov 30   Files VETU and VETB to have open access
 NEWS 25  Dec 10   WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
 NEWS 26  Dec 10   DGENE BLAST Homology Search

 NEWS EXPRESS  August 15 CURRENT WINDOWS VERSION IS V6.0c,
               CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP),
               AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
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=> S IMPLANTS
L1 92198 IMPLANTS

=> S COLLAGEN
L2 233782 COLLAGEN

=> S NERVE (W) REGENERATION
L3 15971 NERVE (W) REGENERATION

=> S L1 AND L2
L4 3929 L1 AND L2

=> S L3 AND L4
L5 69 L3 AND L4

=> D L5 IBIB ABS 1-69

L5 ANSWER 1 OF 69 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:132348 BIOSIS
DOCUMENT NUMBER: PREV200000132348
TITLE: Connective tissue response to tubular **implants** for peripheral **nerve regeneration**: The role of myofibroblasts.
AUTHOR(S): Chamberlain, Lila J.; Yannas, Ioannis V. (1); Hsu, Hu-Ping; Spector, Myron
CORPORATE SOURCE: (1) Department of Mechanical Engineering, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Room 3-332, Cambridge, MA, 02139 USA
SOURCE: Journal of Comparative Neurology., (Feb. 21, 2000) Vol. 417, No. 4, pp. 415-430.
ISSN: 0021-9967.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The presence of contractile cells, their organization around regenerating nerve trunks, and the hypothetical effect of these organized structures on the extent of regeneration across a tubulated 10-mm gap in the rat sciatic nerve were investigated. **Collagen** and silicone tubes were implanted both empty and filled with a **collagen**-glycosaminoglycan (GAG) matrix. Nerves were retrieved at 6, 30, and 60 weeks postoperatively and time-dependent values of the nerve trunk diameter along the tubulated length were recorded. The presence of myofibroblasts was identified immunohistochemically using a monoclonal antibody to alpha-smooth muscle actin. Myofibroblasts were circumferentially arranged around the perimeter of regenerated nerve trunks, forming a capsule which was about 10 times thicker in silicone tubes than in **collagen** tubes. The nerve trunk diameter that formed inside **collagen** tubes was twice as large as that inside silicone tubes. In contrast, the **collagen**-GAG matrix had a relatively small effect on capsule thickness or diameter of regenerate. It was hypothesized that the frequency of successful bridging by axons depends on the balance between two competitive forces: the axial forces generated by the outgrowth of axons and nonneuronal cells from the proximal stump and the constrictive, circumferential forces imposed by the contractile tissue capsule that promote closure of the wounded stumps and prevent axon elongation. Because the presence of the **collagen**-GAG matrix has enhanced greatly the recovery of normal function of

regenerates in silicone tubes, it was hypothesized that it accelerated axonal elongation sufficiently before the hypothetical forces constricting the nerve trunk in silicone tubes became sufficiently large. The combined data suggest a new mechanism for peripheral **nerve regeneration** along a tubulated gap.

L5 ANSWER 2 OF 69 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:451236 BIOSIS
DOCUMENT NUMBER: PREV199800451236
TITLE: Early peripheral nerve healing in **collagen** and silicone tube **implants**: Myofibroblasts and the cellular response.
AUTHOR(S): Chamberlain, L. J.; Yannas, I. V.; Arrizabalaga, A.; Hsu, H.-P.; Norregaard, T. V.; Spector, M. (1)
CORPORATE SOURCE: (1) Dep. Orthop. Surg., Brigham Women's Hosp., Harv. Med. Sch., Boston, MA 02115 USA
SOURCE: Biomaterials, (Aug., 1998) Vol. 19, No. 15, pp. 1393-1403. ISSN: 0142-9612.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Injuries to peripheral nerves innervating a limb cause paralysis, and can necessitate amputation. The inability of the nerves to regenerate spontaneously and the limitations of autograft procedures led to the development of treatments involving insertion of the nerve ends into prosthetic tubular devices. Previous work showed that 'entubulation' of the nerve ends in a silicone tube containing a specific porous, resorbable **collagen**-GAG (CG) copolymer, serving as an analog of extracellular matrix, improved regeneration compared to an empty silicone tube. However, long-term treatment with silicone tubes produced constriction that caused partial degradation of the regenerated axons; for this and other reasons, implementation of a nondegradable tube may require a second surgical procedure for removal. In this study the silicone tube was replaced with porous and non-porous **collagen** tubes in order to produce fully degradable devices. CG-filled **collagen** tubes and controls (CG-filled silicone tubes and empty **collagen** and silicone tubes) were implanted in a 10-mm gap in the rat sciatic nerve, with three rats in each group. The regeneration was evaluated after six weeks using light microscope images of cross sections of the nerve that were digitized and analyzed. Histograms of the diameters of the axons were generated and compared. The cellular response to the implanted biomaterials was assessed histologically, and immunohistochemistry was performed using an antibody to alpha-smooth muscle actin in order to determine the presence of myofibroblasts (contractile cells). Axonal regrowth was comparable in porous **collagen**, non-porous **collagen**, and silicone tubes filled with a CG matrix. These results support the implementation of a degradable **collagen** tube in place of a silicone device. Confirming earlier work, regeneration through the silicone and **collagen** tubes was enhanced by the CG copolymer, compared to empty tubes. A notable finding was a continuous layer of myofibroblasts on the surfaces of all of the six silicone tube prostheses, but on the inner surface of only one of six **collagen** tubes (Fisher's exact tests; $P < 0.01$). This is the first report of contractile capsules around silicone tubes, and supports the use of degradable **collagen** tubes in peripheral **nerve regeneration**. Macrophages were found bordering both the silicone and **collagen** tubes, and in the case of the **collagen** tubes, appeared to be participating in the regulation of the tubes.

L5 ANSWER 3 OF 69 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1996:118186 BIOSIS
DOCUMENT NUMBER: PREV199698690321
TITLE: Recent advances in tissue synthesis in vivo by use of **collagen**- glycosaminoglycan copolymers.
AUTHOR(S): Ellis, D. L.; Yannas, I. V. (1)
CORPORATE SOURCE: (1) Dep. Mech. Eng., 77 Massachusetts Ave., Mass. Inst. Technol., Cambridge, MA 02139 USA
SOURCE: Biomaterials, (1996) Vol. 17, No. 3, pp. 291-299. ISSN: 0142-9612.
DOCUMENT TYPE: General Review

LANGUAGE: English

AB Biologically active analogues of the extracellular matrix (ECM) are synthesized by grafting glycosaminoglycan (GAG) chains onto type I **collagen**, and by controlling the physicochemical properties of the resulting graft copolymer. **Collagen**-GAG ECM analogues have previously been shown to induce regeneration of the dermis in humans and the guinea pig, and of the rat sciatic nerve. Current studies have emphasized elucidation of the molecular mechanism through which tissue-specific ECM analogues induce regeneration. The contribution of the GAGs to the biological activity of the skin regeneration template was confirmed by studying the contribution of several GAGs to the inhibition of wound contraction in guinea pigs. The interaction between cells and the porous structure of an ECM analogue was studied with emphasis on the deformation of pores which occurs during wound contraction. The synthesis of scar, as well as of partly regenerated tissue which has a morphology between that appropriate for scar and for normal dermis, was quantitatively assayed for the first time using a laser light scattering technique. An ECM analogue which has been shown to be capable of inducing regeneration of functional sciatic nerve in the rat over a gap larger than 10 mm was incorporated in the design of a biodegradable implant for peripheral **nerve regeneration**.

L5 ANSWER 4 OF 69 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1994:131333 BIOSIS
DOCUMENT NUMBER: PREV199497144333
TITLE: Labeled Schwann cell transplants versus sural nerve grafts in nerve repair.
AUTHOR(S): Kim, Daniel H. (1); Connolly, Sean E.; Kline, David G.; Voorhies, Rand M.; Smith, Andrea; Powell, Mary; Yoes, Tracy; Daniloff, Joanne K.
CORPORATE SOURCE: (1) Dep. Neurosurg., La. State Univ. Med. Cent., 1542 Tulane Ave., New Orleans, LA 70112 USA
SOURCE: Journal of Neurosurgery, (1994) Vol. 80, No. 2, pp. 254-260.
ISSN: 0022-3085.
DOCUMENT TYPE: Article
LANGUAGE: English

AB This study evaluated the ability of Schwann cell transplants to enhance the recovery of function in injured nerves and compared the results to those produced by sural nerve grafts. Schwann cells were isolated from sciatic nerves, prelabeled with gold fluorescent dye admixed with **collagen** gel, and placed in resorbable **collagen** tubes. Twenty-four adult rats underwent severing of the bilateral sciatic nerves, with a 10-mm gap between the nerve stumps. The rats were then divided into two groups. A **collagen** tube with implanted Schwann cells was implanted in one leg of the Group I rats, and the contralateral leg served as a control and was repaired with a **collagen** tube filled with **collagen** get only. The Group II animals received conduits packed with labeled Schwann cells in one leg to bridge the 10-mm gap; the contralateral leg was repaired with an autogenous sural nerve graft. Recovery of function was assessed physiologically and morphologically. Nerve conduction velocity and nerve action potential amplitude measurements showed that the Schwann cell **implants** induced return of function comparable to that of the sural nerve grafts. Morphological assessments of myelination suggested a tendency toward greater numbers of myelinated axons in Schwann cell **implants** than in sural nerve grafts. Anatomical analyses of gold fluorescent dye showed both high viability of prelabeled Schwann cells at 120 days after transplantation and migration as far as 30 mm away from the implant site.

L5 ANSWER 5 OF 69 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1990:285361 BIOSIS
DOCUMENT NUMBER: BA90:16207
TITLE: IMMUNOGENICITY OF COLLAGENOUS **IMPLANTS**.
AUTHOR(S): MEADE K R; SILVER F H
CORPORATE SOURCE: BIOMATERIALS CENT., DEP. PATHOL., UMDNJ-ROBERT WOOD JOHNSON MED. SCH., 675 HOES LANES, PISCATAWAY, N.J. 08854, USA.
SOURCE: BIOMATERIALS, (1990) 11 (3), 176-180.
CODEN: BIMADU. ISSN: 0142-9612.

FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Collagenous biomaterials have been used in our laboratory for treatment of decubitus ulcers, tendon/ligament repair and **nerve regeneration**. Results of previous studies suggest that **implants** containing bovine type I **collagen** enhance repair and regeneration of connective tissue found in different organs. The purpose of this paper is to evaluate the immunological response to type I **collagen** that is cross-linked using either glutaraldehyde or cyanamide treatment. Humoral and cell mediated responses to type I **collagen** are evaluated in a rabbit model. Results obtained in this study suggest that antibody levels and cell-mediated response to type I **collagen** are highest in animals exposed to uncross-linked implant material and these responses are increased by booster injections of the antigen. Antibody titres to cross-linked **collagen** are significantly lower than those observed for uncross-linked material. Extensive implant cross-linking does not totally eliminate the humoral response and may lead to a cell-mediated reaction.

L5 ANSWER 6 OF 69 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:564876 CAPLUS
DOCUMENT NUMBER: 135:142300
TITLE: Gel-infused polymeric sponges for tissue repair and augmentation
INVENTOR(S): Bentz, Hanne; Garcia, A. Minerva; Hubbell, Jeffrey A.
PATENT ASSIGNEE(S): Orthogene, Inc., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001054735	A2	20010802	WO 2001-US2837	20010126

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-178646 P 20000128
AB Gel-infused sponge matrix comprising an absorbable sponge material, a gel and an active ingredient are disclosed, as are methods of enhancing tissue repair, regeneration or augmentation using the gel-infused sponge. A sponge material is selected from **collagens**, polysaccharides, synthetic polymers, or hyaluronic acid, while a gel precursor is a fibrinogen, thrombin, or serum albumin. For example, gels of low crosslink d. and/or low protein or gel precursor concn., that would form only weak gels by themselves formed a more cohesive and stronger material when added into a sponge and retain enough porosity to be remodeled into the new tissue, such as bone.

filling material

L5 ANSWER 7 OF 69 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:456002 CAPLUS
DOCUMENT NUMBER: 135:262194
TITLE: **Collagen** filaments as a scaffold for **nerve regeneration**
AUTHOR(S): Yoshii, Satoru; Oka, Masanori
CORPORATE SOURCE: Institute of Biomedical Engineering, Kansai Denryoku Hospital, Osaka, 553-0003, Japan
SOURCE: J. Biomed. Mater. Res. (2001), 56(3), 400-405
CODEN: JBMRBG; ISSN: 0021-9304
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal

chart to look

LANGUAGE: English

AB This article describes repair of peripheral nerve defect using **collagen** filaments instead of tubes. Many tube-shaped nerve guides induce regeneration of severed peripheral nerve axons within a limited distance. Substantial regeneration of nerve axons has not been reported without a tubular conduit. Here the regeneration of peripheral nerve axons along filaments of **collagen** without a tube was shown. Cables of **collagen** filaments were grafted to repair 20 mm defects of rat sciatic nerves. Nerve autografts and **collagen** tubes were grafted as controls. The mean no. and the mean fiber diam. of regenerated myelinated axons were approx. 4800 and 3.3 .mu.m in the distal end of the nerve autograft at 8 wk postoperatively while in the distal end of the **collagen**-filaments nerve guide, they were approx. 5500 and 2.3 .mu.m. **Collagen** tubes failed to bridge the nerve defect. Histol. studies suggest that nerve axons regenerated substantially along the **collagen** filaments.

filaments of collagen for 1:6

REFERENCE COUNT: 26

REFERENCE(S): (1) Ansselin, A; Neuropathol Appl Neurobiol 1997, V23, P387 MEDLINE
(2) Archibald, S; J Comp Neurol 1991, V306, P685 MEDLINE
(3) Bain, J; Plast Reconstr Surg 1989, V83, P129 MEDLINE
(10) Henry, E; Exp Neurol 1985, V90, P652 CAPLUS
(19) Madison, R; Brain Res 1988, V447, P325 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 69 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:4624 CAPLUS
DOCUMENT NUMBER: 135:200222
TITLE: Bioartificial peripheral nerve guide tube
AUTHOR(S): Shimizu, Ysuhiko
CORPORATE SOURCE: Institute of Medical Science, Kyoto University, Japan
SOURCE: Igaku no Ayumi (2000), 195(3), 184-187
CODEN: IGAYAY; ISSN: 0039-2359
PUBLISHER: Ishiyaku Shuppan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review with 7 refs. on artificial peripheral nerve guide tubes, covering characteristics of gelatin, **collagen**, **collagen** /polyglycolic acid composite, and laminin-coated **collagen** /polyglycolic acid composite nerve guide tubes.

L5 ANSWER 9 OF 69 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:422742 CAPLUS
DOCUMENT NUMBER: 133:155335
TITLE: Peripheral **nerve regeneration** using silicone rubber chambers filled with **collagen**, laminin and fibronectin
AUTHOR(S): Chen, Yueh-Sheng; Hsieh, Ching-Liang; Tsai, Chin-Chuan; Chen, Ter-Hsin; Cheng, Wen-Chiang; Hu, Cheng-Li; Yao, Chun-Hsu
CORPORATE SOURCE: Institute of Chinese Medical Science, China Medical College, Taichung, Taiwan
SOURCE: Biomaterials (2000), 21(15), 1541-1547
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

103 for filling material collagen laminin

AB A 10 mm gap of rat sciatic nerve was created between the proximal and distal nerve stumps, which were sutured into silicone rubber tubes filled with an extracellular gel contg. **collagen**, laminin and fibronectin. Empty silicone rubber tubes were used as controls. Six weeks after implantation, all extracellular elements were completely degraded and absorbed, and 90% of the animals from the extracellular gel group exhibited regeneration across the nerve gaps, whereas only 60% in the control group. Both qual. and quant. histol. of the regenerated nerves revealed a more mature ultrastructural organization with 28% larger cross-sectional area and 28% higher no. of myelinated axons in the

extracellular gel group than the controls. The gel mixt. of **collagen**, laminin and fibronectin could offer a suitable growth medium for the regeneration of axons.

REFERENCE COUNT: 41

REFERENCE(S):
(2) Aldini, N; Biomaterials 1996, V17, P959 CAPLUS
(4) Bailey, S; J Neurocytol 1993, V22, P176 CAPLUS
(5) Baldwin, S; Int J Dev Neurosci 1996, V14, P351 CAPLUS
(6) Baron-Van Evercooren, A; J Cell Biol 1982, V93, P211 CAPLUS
(7) Borkenhagen, M; Biomaterials 1998, V19, P2155 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 69 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:404964 CAPLUS

DOCUMENT NUMBER: 133:140176

TITLE: Near-terminus axonal structure and function following rat sciatic **nerve regeneration** through a **collagen**-GAG matrix in a ten-millimeter gap

AUTHOR(S): Chamberlain, L. J.; Yannas, I. V.; Hsu, H-P.; Strichartz, G. R.; Spector, M.

CORPORATE SOURCE: Department of Mechanical Engineering, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA

SOURCE: J. Neurosci. Res. (2000), 60(5), 666-677
CODEN: JNREDK; ISSN: 0360-4012

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The objectives of this study were to evaluate the regenerated axon structure at near-terminal locations in the peroneal and tibial branches 1 yr following implantation of several tubular devices in a 10-mm gap in the adult rat sciatic nerve and to det. the extent of recovery of selected sensory and motor functions. The devices were **collagen** and silicone tubes implanted alone or filled with a porous **collagen** -glycosaminoglycan matrix. Intact contralateral nerves and autografts were used as controls. Nerves were retrieved at 30 and 60 wk postoperatively for histol. evaluation of the no. and diam. of regenerated axons proximal and distal to the gap and in the tibial and peroneal nerve branches, near the termination point. Several functional evaluation methods were employed: gait anal., pinch test, muscle circumference, and response to elec. stimulation. A notable finding was that the matrix-filled **collagen** tube group had a significantly greater no. of large-diam. myelinated axons (.gtoreq.6 .mu.m in diam.) in the distal nerve branches than any other group, including the autograft group. These results were consistent with previously reported electrophysiol. measurements that showed that the action potential amplitude for the A fibers in the matrix-filled **collagen** tube group was greater than for the autograft control group. Functional testing revealed the existence of both sensory and motor recovery following peripheral **nerve regeneration** through all devices; however, the tests employed in this study did not show differences among the groups with regeneration. Elec. stimulation in vivo showed that threshold parameters to elicit muscle twitch were the same for reinnervating and control nerves. The investigation is of importance in showing for the first time the superiority of a specific fully resorbable off-the-shelf device over an autograft for bridging gaps in peripheral nerve, with respect to the near-terminus axonal structure.

filling mate

REFERENCE COUNT: 44

REFERENCE(S):
(5) Archibald, S; J Neurosci 1995, V15, P4109 CAPLUS
(9) Chamberlain, L; Exp Neurol 1998, V154, P315 CAPLUS
(10) Chamberlain, L; Tissue Engr 1997, V3, P353 CAPLUS
(11) Chamberlain, L; Tissue engineering methods and protocols 1999, P3 CAPLUS
(13) Chang, A; Proc ACS Div Polymeric Materials Sci Engr 1988, V59, P906 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 69 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:400378 CAPLUS
DOCUMENT NUMBER: 133:155361
TITLE: Peripheral **nerve regeneration** across an 80-mm gap bridged by a polyglycolic acid (PGA)-**collagen** tube filled with laminin-coated **collagen** fibers: a histological and electrophysiological evaluation of regenerated nerves
AUTHOR(S): Matsumoto, K.; Ohnishi, K.; Kiyotani, T.; Sekine, T.; Ueda, H.; Nakamura, T.; Endo, K.; Shimizu, Y.
CORPORATE SOURCE: Institute for Frontier Medical Sciences, Department of Bioartificial Organs, Kyoto University, Kyoto, 606-8507, Japan
SOURCE: Brain Res. (2000), 868(2), 315-328
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

collagen tube filling material

AB We evaluated peripheral **nerve regeneration** across an 80-mm gap using a novel artificial nerve conduit. The conduit was made of a polyglycolic acid (PGA)-**collagen** tube filled with laminin-coated **collagen** fibers. Twelve beagle dogs underwent implantation of the nerve conduit across an 80-mm gap in the left peroneal nerve. In 4 other dogs used as neg. controls, the nerve was resected and left unconnected. Histol. observation showed that numerous unmyelinated and myelinated nerve fibers, all smaller in diam. and with a thinner myelin sheath than normal nerve fibers, regrew through and beyond the gap 12 mo after implantation. The distribution of the regenerated axonal diams. was different from that of the normal axonal diams. Compd. muscle action potentials, motor evoked potentials, and somatosensory evoked potentials were recorded in most animals 3 mo after implantation. Peak amplitudes and latencies recovered gradually, which indicating the functional establishment of the nerve connection with the target organs. In addn. to the ordinary electrophysiol. recoveries, potentials with distinct latencies originating from A.alpha., A.delta. and C fibers became distinguishable at the 6th lumbar vertebra following stimulation of the peroneal nerve distal to the gap 12 mo after implantation. The pattern of walking without load was restored to almost normal 10-12 mo after implantation. Neither electrophysiol. nor histol. restoration was obtained in the controls. Our nerve conduit can guide peripheral nerve elongation and lead to favorable functional recovery across a wider nerve gap than previously reported artificial nerve conduits.

REFERENCE COUNT: 35
REFERENCE(S): (2) Archibald, S; J Neurosci 1995, V15, P4109 CAPLUS
(6) Chamberlain, L; Exp Neurol 1998, V154, P315 CAPLUS
(9) Evans, G; Biomaterials 1999, V20, P1109 CAPLUS
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(11) Ide, C; Exp Neurol 1998, V154, P99 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 69 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:452508 CAPLUS
DOCUMENT NUMBER: 132:98057
TITLE: Magnetically aligned **collagen** gel filling a **collagen** nerve guide improves peripheral **nerve regeneration**
AUTHOR(S): Ceballos, Dolores; Navarro, Xavier; Dubey, Naren; Wendelschafer-Crabb, Gwen; Kennedy, William R.; Tranquillo, Robert T.
CORPORATE SOURCE: Department of Neurology, University of Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Exp. Neurol. (1999), 158(2), 290-300
CODEN: EXNEAC; ISSN: 0014-4886
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

☆ dub

Collagen tube w/ collagen gel

AB Bioresorbable **collagen** nerve guides filled with either magnetically aligned type I **collagen** gel or control

collagen gel were implanted into 4- or 6-mm surgical gaps created in the sciatic nerve of mice and explanted 30 and 60 days postoperation (dpo) for histol. and immunohistochem. evaluation. The hypothesis was that contact guidance of regenerating axons and/or invading nonneuronal cells to the longitudinally aligned **collagen** fibrils would improve **nerve regeneration**. The criterion for regeneration was observation of regenerating myelinated fibers distal to the nerve guide. Consistent with previous studies showing poor regeneration in 6-mm gaps at 60 dpo with entubulation repair, only one of six mice exhibited regeneration with control **collagen** gel. In contrast, four of four mice exhibited regeneration with magnetically aligned **collagen** gel, including the appearance of nerve fascicle formation. The nos. of myelinated fibers were less than the uninjured nerve in all groups, however, which may have been due to rapid resorption of the nerve guides. An attempt to increase the stability of the **collagen** gel, and thereby the directional information presented by the aligned **collagen** fibrils, by crosslinking the **collagen** with ribose before implantation proved detrimental for regeneration. (c) 1999 Academic Press.

REFERENCE COUNT: 48

REFERENCE(S):
(3) Archibald, S; J Neurosci 1995, V15, P4109 CAPLUS
(8) Girton, T; J Biomed Mat Res 1999, V46, P87 CAPLUS
(13) Henry, E; Exp Neurol 1985, V90, P652 CAPLUS
(15) King, G; Endocrinol Metab Clin North Am 1996, V25, P255 CAPLUS
(16) Labrador, R; Exp Neurol 1998, V149, P243 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 69 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:192735 CAPLUS

DOCUMENT NUMBER: 131:23475

TITLE: Evaluation of several techniques to modify denatured muscle tissue to obtain a scaffold for peripheral **nerve regeneration**

AUTHOR(S): Meek, Marcel F.; Den Dunnen, Wilfred F. A.; Schakenraad, Jeff M.; Robinson, Peter H.

CORPORATE SOURCE: Center for Artificial Organs, Division of Biomaterials, University of Groningen, Groningen, 9712 KZ, Neth.

SOURCE: Biomaterials (1999), 20(5), 401-408
CODEN: BIMADU; ISSN: 0142-9612

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The aim of this study was to (1) evaluate the effect of several prepn. techniques of denatured muscle tissue to obtain an open 3-dimensional structure, and (2) test if this scaffold is suitable for peripheral **nerve regeneration**. Four samples (A-D) of muscle tissue specimens were evaluated using light microscopy, immunohistochem. and cryo-SEM. Sample C showed the most open extracellular matrix, while **collagen** type IV and laminin (in the basal lamina) could still be obsd. by immunohistochem. An in vivo pilot study showed that the first signs of functional nerve recovery and axon regeneration could be obsd. after 3 wk of implantation. Thus, sample C has the most open structure and leads to good **nerve regeneration** and functional nerve recovery.

REFERENCE COUNT: 21

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(6) Den Dunnen, W; J Biomed Mater Res 1997, V36, P337 CAPLUS
(7) Den Dunnen, W; J Mater Sci:Mat Med 1993, V4, P521 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 69 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:66603 CAPLUS
DOCUMENT NUMBER: 130:286972
TITLE: **Collagen**-GAG substrate enhances the quality of **nerve regeneration** through **collagen** tubes up to level of autograft
AUTHOR(S): Chamberlain, L. J.; Yannas, I. V.; Hsu, H-P.; Strichartz, G.; Spector, M.
CORPORATE SOURCE: Department of Mechanical Engineering, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA
SOURCE: Exp. Neurol. (1998), 154(2), 315-329
CODEN: EXNEAC; ISSN: 0014-4886
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Peripheral **nerve regeneration** was studied across a tubulated 10-mm gap in the rat sciatic nerve using histomorphometry and electrophysiol. measurements of A-fiber, B-fiber, and C-fiber peaks of the evoked action potentials. Tubes fabricated from large-pore **collagen** (max. pore diam., 22 nm), small-pore **collagen** (max. pore diam., 4 nm), and silicone were implanted either saline-filled or filled with a highly porous, **collagen**-glycosaminoglycan (CG) matrix. The CG matrix was deliberately synthesized, based on a previous optimization study, to degrade with a half-life of about 6 wk and to have a very high sp. surface through a combination of high pore vol. fraction (0.95) and relatively small av. pore diam. (35 .mu.m). Nerves regenerated through tubes fabricated from large-pore **collagen** and filled with the CG matrix had significantly more large-diam. axons, more total axons, and significantly higher A-fiber conduction velocities than any other tubulated group; and, although lower than normal, their histomorphometric and electrophysiol. properties were statistically indistinguishable from those of the autograft control. Although the total no. of myelinated axons in nerves regenerated by tubulation had reached a plateau by 30 wk, the no. of axons with diam. larger than 6.mu.m, which have been uniquely assocd. with the A-fiber peak of the action potential, continued to increase at substantial rates through the completion of the study (60 wk). The kinetic data strongly suggest that a nerve trunk maturation process, not previously reported in studies of the tubulated 10-mm gap in the rat sciatic nerve, and consisting in increase of axonal tissue area with decrease in total tissue area, continues beyond 60 wk after injury, resulting in a nerve trunk which increasingly approaches the structure of the normal control. (c) 1998 Academic Press.

REFERENCE COUNT: 62
REFERENCE(S): (4) Aldini, N; Biomaterials 1996, V17, P959 CAPLUS
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(15) Chamberlain, L; Biomaterials 1998, V19, P1393 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 69 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:769882 CAPLUS
DOCUMENT NUMBER: 130:158369
TITLE: Evaluation of **collagen** nerve guide in facial **nerve regeneration**
AUTHOR(S): Kitahara, Americo K.; Suzuki, Yoshihisa; Nishimura, Yoshihiko; Suzuki, Kyoko; Kiyotani, Tetsuya; Takimoto, Yukinobu; Nakamura, Tatsuo; Shimizu, Yasuhiko; Endo, Katsuaki
CORPORATE SOURCE: Department of Plastic and Reconstructive Surgery. Faculty of Medicine, Kyoto University, Kyoto, 606-8507, Japan
SOURCE: J. Artif. Organs (1998), 1(1), 22-27
CODEN: JAORFN; ISSN: 1434-7229
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Facial nerve paralysis due to resection of tumors or as a consequence of trauma is a frequently obsd. complication. Thus, in the present study, we evaluated a **collagen** nerve guide in facial **nerve regeneration** across a 5-mm nerve gap. This biol. tube was manufd. from 3% **collagen**, coated over a Teflon tube used only as a template and submitted to thermal dehydration at 105.degree. for 24h. The **collagen** tube was implanted at the dorsal ramous of the facial nerve of 5 adult cats over a gap of 5 mm. The facial nerve of the contralateral side was kept intact and used as control. Electrophysiol. study was performed from 3 wk after surgery, and histol. and horseradish peroxidase labeling examn. was carried out 8 wk after implantation. Electrophysiol. study confirmed the recovery of elec. activity of the **collagen**-implanted regenerated nerve. Light-microscopic examn. of **collagen** tube-implanted specimens revealed a well vascularized regenerated nerve, which under an electron microscope showed many myelinated axons surrounded by Schwann cells and unmyelinated axons. Horseradish peroxidase staining demonstrated labeling of facial motoneurons in the brainstem and facial nerve terminals in the neuromuscular junction, also confirming restoration of the whole facial nerve tract from the reinnervated muscles, passing through the regenerated site to the brainstem. The **collagen** tube was very efficient as a nerve guide over a 5-mm facial nerve gap and shows great promise as a nerve conduit.

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REFERENCE(S): (1) Archibald, S; J Comp Neurol 1991, V306, P685 MEDLINE
(2) Archibald, S; J Neurosci 1995, V15, P4109 CAPLUS
(5) Den Dunnen, W; J Biomed Mater Res 1995, V29, P757 CAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 69 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:681326 CAPLUS
DOCUMENT NUMBER: 130:47863

TITLE: **Collagen** containing neurotrophin-3 (NT-3) attracts regrowing injured corticospinal axons in the adult rat spinal cord and promotes partial functional recovery

AUTHOR(S): Houweling, D. A.; Lankhorst, A. J.; Gispen, W. H.; Bar, P. R.; Joosten, E. A. J.
CORPORATE SOURCE: Department of Neurology, Rudolf Magnus Institute for Neurosciences, Utrecht University, Utrecht, 3508 GA, Neth.

SOURCE: Exp. Neurol. (1998), 153(1), 49-59
CODEN: EXNEAC; ISSN: 0014-4886
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB During development, neurotrophic factors play an important role in the guidance and outgrowth of axons. Our working hypothesis is that neurotrophic factors involved in the development of axons of a particular CNS tract are among the most promising candidates for stimulating and directing the regrowth of fibers of this tract in the lesioned adult animal. The neurotrophin NT-3 is known to be involved in the target selection of outgrowing corticospinal tract (CST) fibers. We studied the capacity of locally applied NT-3 to stimulate and direct the regrowth of axons of the CST in the lesioned adult rat spinal cord. We also studied the effect of NT-3 application on the functional recovery of rats after spinal cord injury, using the gridwalk test. NT-3 was applied at the site of the lesion dissolved into rat tail **collagen** type I. Four weeks after spinal cord injury and **collagen** implantation, significantly more CST fibers had regrown into the **collagen** matrix contg. NT-3 (22%) than into the control **collagen** matrix without NT-3 (7%). No CST fibers grew into areas caudal to the **collagen** implant. Despite the absence of regrowth of corticospinal axons into host tissue caudal to the lesion area, functional recovery was obsd. in rats with NT-3 contg. **collagen**

filling material in nerve gap to stimulate

implants. (c) 1998 Academic Press.
REFERENCE COUNT: 42
REFERENCE(S): (1) Altar, C; J Neurosci 1993, V13, P733 CAPLUS
(2) Bastmeyer, M; J Neurosci 1996, V16, P1450 CAPLUS
(3) Bottenstein, J; Proc Natl Acad Sci U S A 1979, V76, P514 CAPLUS
(4) Cohen, R; J Neurosci 1996, V16, P6433 CAPLUS
(5) Condorelli, D; J Neurochem 1994, V63, P509 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 69 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:597145 CAPLUS
DOCUMENT NUMBER: 129:321115
TITLE: Early peripheral nerve healing in **collagen** and silicone tube **implants**: myofibroblasts and the cellular response
AUTHOR(S): Chamberlain, L. J.; Yannas, I. V.; Arrizabalaga, A.; Hsu, H.-P.; Norregaard, T. V.; Spector, M.
CORPORATE SOURCE: Department of Mechanical Engineering, Massachusetts Inst. of Technology, Cambridge, MA, 02139, USA
SOURCE: Biomaterials (1998), 19(15), 1393-1403
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Injuries to peripheral nerves innervating a limb cause paralysis, and can necessitate amputation. The inability of the nerves to regenerate spontaneously and the limitations of autograft procedures led to the development of treatments involving insertion of the nerve ends into prosthetic tubular devices. Previous work showed that 'entubulation' of the nerve ends in a silicone tube contg. a specific porous, resorbable **collagen**-GAG (CG) copolymer, serving as an analog of extracellular matrix, improved regeneration compared to an empty silicone tube. However, long-term treatment with silicone tubes produced constriction that caused partial degrdn. of the regenerated axons, for this and other reasons, implementation of a nondegradable tube may require a second surgical procedure for removal. In this study the silicon tube was replaced with porous and non-porous **collagen** tubes in order to produce fully degradable devices. CG-filled **collagen** tubes and controls (CG-filled silicone tubes and empty **collagen** and silicone tubes) were implanted in a 10-mm gap in the rat sciatic nerve, with three rats in each group. The regeneration was evaluated after six weeks using light microscope images of cross sections of the nerve that were digitized and analyzed. Histograms of the diams. of the axons were generated and compared. The cellular response to the implanted biomaterials was assessed histol., and immunohistochem. was performed using an antibody to .alpha.-smooth muscle actin in order to det. the presence of myofibroblasts (contractile cells). Axonal regrowth was comparable in porous **collagen**, non-porous **collagen**, and silicon tubes filled with a CG matrix. These results support the implementation of a degradable **collagen** tube in place of a silicone device. Confirming earlier work, regeneration through the silicone and **collagen** tubes was enhanced by the CG copolymer, compared to empty tubes. A notable finding was a continuous layer of myofibroblasts on the surfaces of all of the six silicone tube prostheses, but on the inner surface of only one of six **collagen** tubes (Fisher's exact tests; $P < 0.01$). This is the first report of contractile capsules around silicone tubes, and supports the use of degradable **collagen** tubes in peripheral **nerve regeneration**. Macrophages were found bordering both the silicone and **collagen** tubes, and in the case of the **collagen** tubes appeared to be participating in the regulation of the tubes.

L5 ANSWER 18 OF 69 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:367319 CAPLUS
DOCUMENT NUMBER: 122:230597
TITLE: A synthetic laminin peptide is active in peripheral **nerve regeneration** in vivo
AUTHOR(S): Takakuda, Kazuo; Miyairi, Hiroo; Itou, Souichirou;

O(hta, Tuyoshi; Samejima, Hirotake
CORPORATE SOURCE: Inst. Med. Dent. Eng., Tokyo Med. Dent. Univ., Tokyo, 101, Japan
SOURCE: Iyo Kizai Kenkyusho Hokoku (Tokyo Ika Shika Daigaku) (1994), 28, 70-4
CODEN: IKKHBS; ISSN: 0082-4739
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB The activity of synthetic laminin peptides, which contain YIGSR or IKVAV sequences, were examd. in a **nerve regeneration** model in vivo. A segment of a rat sciatic nerve was replaced by a 15 mm long silicone tube filled with either **collagen** gel, laminin-contg. **collagen** gel, laminin- and YIGSR peptide-contg. **collagen** gel, YIGSR peptide-contg. **collagen** gel, laminin and IKVAV peptide-contg. **collagen** gel, or IKVAV peptide-contg. **collagen** gel. At 2, 4, 6, 8, and 10 wk after surgery, the **implants** were retrieved and histol. examd. by light and electron microscopy. Many regenerated axons were found in the tubes filled with the laminin-contg. **collagen** gel, whereas none in the ones with **collagen** gel alone. When the YIGSR peptide was applied with laminin, it inhibited **nerve regeneration**; however, without laminin, it enhanced regeneration. The IKVAV peptide showed no inhibitory or enhancing effects. The authors concluded that the main functional domain of laminin in **nerve regeneration** is the YIGSR sequence, and this synthetic peptide may be used as a growth guidance agent in neural prostheses.

laminin in collagen

L5 ANSWER 19 OF 69 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:491907 CAPLUS
DOCUMENT NUMBER: 121:91907
TITLE: nerve and blood vessel grafts prepared from fetal membranes
INVENTOR(S): Shenaq, Saleh M.; Gray, Kathy Jo
PATENT ASSIGNEE(S): Research Development Foundation, USA
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 14 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1079912	A	19931229	CN 1992-114817	19921126
IL 103893	A1	19970218	IL 1992-103893	19921126

PRIORITY APPLN. INFO.: US 1991-799517 19911126

AB Fetal membranes (amniotic membranes) are made into tube structures in which at least 1 layer in the tube wall contains type I, II, and III **collagens** from placeta. The prepns. are useful as nerve and blood vessel grafts and promoted the **nerve regeneration**.

L5 ANSWER 20 OF 69 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:484898 CAPLUS
DOCUMENT NUMBER: 113:84898
TITLE: Prosthesis for promotion of **nerve regeneration** based on **collagen**
INVENTOR(S): Yannas, Ioannis V.; Orgill, Dennis P.; Loree, Howard M., II; Kirk, James F.; Chang, Albert S. P.; Mikic, Borivoje B.; Krarup, Christian; Norregaard, Thorkild Vad; Zervas, Nicholas T.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 8910728	A1	19891116	WO 1989-US1916	19890505
W: JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
PRIORITY APPLN. INFO.:			US 1988-191415	19880509
			US 1989-327530	19890323

AB A template for axon tissue regeneration is manufd. by introduction of a biodegradable polymer, preferably a **collagen**-glycosaminoglycan, as an aq. suspension into a tubular mold which is placed in a cooling bath to freeze the suspension axially along the mold to provide a preferentially oriented aq. phase within the frozen suspension and then vacuum-dried to form a porous biodegradable template having a preferentially oriented pore structure. Bovine hide **collagen** and chondroitin 6-sulfate from shark cartilage were placed in pH 3 HOAc to form freeze-dried plugs (25 .times. 1.5 mm) in a 90:10 **collagen** /chondroitin ratio as described above. The plugs were highly crosslinked by dehydrothermal treatment (105.degree./100 mTorr, 24 h), glutaraldehyde-treated (24 h), washed, ends cut to make 15 mm tubes, and implanted to connect several ends of siratic nerves in rats. After 6 wk, significantly greater **nerve regeneration** was obsd. than with controls not exposed to the **collagen**-glycosaminoglycan prepn., although considerable variability was obsd.

L5 ANSWER 21 OF 69 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:237190 CAPLUS
DOCUMENT NUMBER: 110:237190
TITLE: Biomaterials for artificial skin and **implants** containing acetylated chitosan, **collagens**, and glycosaminoglycans
INVENTOR(S): Collombel, Christian; Damour, Odile; Gagnieu, Christian; Poinsignon, Frederique; Echinard, Christian; Marichy, Jacques
PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique, Fr.
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 296078	A1	19881221	EP 1988-420194	19880614
EP 296078	B1	19910529		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2616318	A1	19881216	FR 1987-8752	19870615
WO 8810123	A1	19881229	WO 1988-FR303	19880614
W: JP, US				
JP 02500723	T2	19900315	JP 1988-505081	19880614
AT 63825	E	19910615	AT 1988-420194	19880614
US 5166187	A	19921124	US 1989-314508	19890215
PRIORITY APPLN. INFO.:			FR 1987-8752	19870615
			EP 1988-420194	19880614
			WO 1988-FR303	19880614

AB Biomaterials comprise .gtoreq.1 compns. contg. a complex of **collagen**, acetylated chitosan (degree of acetylation .apprx.10-40), and glycosaminoglycans. **Collagen** (1% wt./vol.) was dissolved in 0.05M AcOH at pH 3.5, purified shrimp-shell chitosan was added to give a soln. contg. 15% by wt. chitosan with resp. to **collagen**, and a mixt. of chondroitin 4- and 6-sulfate was added to give a soln. contg. 6% by wt. chondroitin sulfate with resp. to **collagen**. The homogeneous mixt. was adjusted to pH 6.5-7 using Tris-HCl, lyophilized, sterilized, and packaged in plastic pouches contg. 70% alc. An artificial dermis comprising human **collagen**, chondroitin sulfate, glycosaminoglycans, and a biodegradable pseudoepidermis sterilized in 70% alc. showed an elongation of 20.1 mm and a Young's modulus of 0.29 kg/cm2 under a force of 0.23 da N. An artificial dermis of this type was inserted into a cut on the back of rats and sutures were applied; after 2 days a normal inflammatory reaction was

obsd., followed by cell colonization after 7 days.

L5 ANSWER 22 OF 69 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1987:605246 CAPLUS
DOCUMENT NUMBER: 107:205246
TITLE: High molecular weight bioresorbable polymers and implantation devices, especially for promotion of nerve growth
INVENTOR(S): Mares, Frank; Tang, Reginald Ting Hong; Chiu, Tin Ho; Largman, Theodore
PATENT ASSIGNEE(S): Allied Corp., USA
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 226061	A2	19870624	EP 1986-116047	19861120
EP 226061	A3	19880720		
EP 226061	B1	19940216		
R: CH, DE, GB, LI				
JP 62144663	A2	19870627	JP 1986-298597	19861215
JP 05052749	B4	19930806		

PRIORITY APPLN. INFO.: US 1985-809978 19851217
AB Prosthetic **implants** for encouraging cellular growth and regeneration of function, esp. for nerve tissue, consist of a bioresorbable polymer (mol. wt. .gtoreq.150,000). Mouse sciatic nerves (from 3 individuals) were severed and the ends were sutured and inserted into a 5-6 mm nerve guide tube of the invention (DL-lactic acid homopolymer) to give a gap of 3-4 mm. The no. of myelinated axons, detd. by computer, was 1457 .+-. 124 and 1844 .+-. 429 after 4 wks and 6 wks, resp., for a polymer with mol. wt. 234,000.

L5 ANSWER 23 OF 69 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1985:547113 CAPLUS
DOCUMENT NUMBER: 103:147113
TITLE: Polymeric template facilitates regeneration of sciatic nerve across 15mm gap
AUTHOR(S): Yannas, I. V.; Orgill, D. P.; Silver, J.; Norregaard, T. V.; Zervas, N. T.; Schoene, W. C.
CORPORATE SOURCE: Fibers Polym. Lab., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Polym. Mater. Sci. Eng. (1985), 53, 216-18
CODEN: PMSEDG; ISSN: 0743-0515
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The noncellular **collagen**-glycosaminoglycan (CG) polymers induced regeneration of well-vascularized nerve tissue over a gap as large as 15-mm in the rat sciatic nerve. The new tissue which bridged the nerve gap (with CG test **implants**) had a cross-section area 40-110-fold larger than that obtained with the controls (no CG) and was considerably more diverse morphol. than the controls. The test grafts contained myelinated and unmyelinated axons along the length of the regenerated tissue strand. The newly formed tissue in the test **implants** was well vascularized. Evidently highly porous, biodegradable CG polymers, free of exogenous growth factors, can be used to induce regeneration of tissues other than the dermis and the epidermis.

L5 ANSWER 24 OF 69 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1982:593704 CAPLUS
DOCUMENT NUMBER: 97:193704
TITLE: Catecholamine fiber regeneration across a **collagen** bioimplant after spinal cord transection
AUTHOR(S): De la Torre, J. C.
CORPORATE SOURCE: Med. Sch., Northwestern Univ., Chicago, IL, 60611, USA

SOURCE: Brain Res. Bull. (1982), 9(1-6), 545-52
CODEN: BRBUDU; ISSN: 0361-9230
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A cell-free bovine-derived **collagen** matrix was used to study potential axonal regeneration in the transected rat spinal cord. Rats were initially subjected to a 200 g/cm force acceleration injury at T10 and 10 days later, the spinal cord was totally transected at the injury site. Controls had their spinal cord stumps juxtaposed end to end following transection. Exptl. rats had 3-4 mm of spinal cord tissue trimmed from the proximo-distal stumps. The semifluid **collagen** materials was implanted to bridge the proximo-distal ends and after several hours, the **collagen** graft polymd. to a firm gel. Rats were obsd. for 90 days. After 90 days, animals were evaluated using somatosensory evoked potentials, local spinal cord blood flow, and catecholamine histofluorescence in and around the site of transection. The **collagen** bioimplant can support the development of anastomotic blood vessels with the cord as well as provide a nonhostile environment to regenerating spinal cord axons.

L5 ANSWER 25 OF 69 MEDLINE
ACCESSION NUMBER: 2001406046 MEDLINE
DOCUMENT NUMBER: 21349718 PubMed ID: 11457428
TITLE: Reinnervation of a denervated skeletal muscle by spinal axons regenerating through a **collagen** channel directly implanted into the rat spinal cord.
AUTHOR: Kassar-Duchossoy L; Duchossoy Y; Rhrich-Haddout F; Horvat J C
CORPORATE SOURCE: Laboratoire de Neurobiologie, Universite Rene Descartes, 45 rue des Saints-Peres, Paris, France..
duchossoy@im3.inserm.fr
SOURCE: BRAIN RESEARCH, (2001 Jul 20) 908 (1) 25-34.
Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010924
Last Updated on STN: 20010924
Entered Medline: 20010920

AB In the present study, the continuity between the central nervous system (CNS) and the peripheral nervous system (PNS) was restored by mean of a **collagen** channel in order to reinnervate a skeletal muscle. Three groups of animals were considered. In the first group, one end of the **collagen** channel was implanted in the cervical spinal cord of adult rats. The other end was connected to a 30-mm autologous peripheral nerve graft (PNG) implanted into the denervated biceps brachii muscle. The gap between the spinal cord and the proximal nerve stump varied from 3 to 7 mm. In the second group of animals, the distal end of the PNG graft was ligatured in order to compare the survival of the growing axons in the presence and in the absence of a muscular target. In the third group of animals, the extraspinal stump of the **collagen** channel was ligatured. Our study demonstrates that spinal neurons and dorsal root ganglion (DRG) neurons can grow long axons through the **collagen** channel over a 7-mm gap and reinnervate a denervated skeletal muscle. The results also indicate that the presence of a PNG at the extraspinal stump of the **collagen** channel is essential for axonal regrowth and that the muscle target contributes to the long-term maintenance of the regenerating axons. These data might be interesting for clinical application when the continuity between the CNS and PNS is interrupted such as in root avulsion.

L5 ANSWER 26 OF 69 MEDLINE
ACCESSION NUMBER: 2001385826 MEDLINE
DOCUMENT NUMBER: 21333500 PubMed ID: 11440435
TITLE: Regrowth of the rostral spinal axons into the caudal ventral roots through a **collagen** tube implanted into hemisected adult rat spinal cord.

AUTHOR: Liu S; Said G; Tadie M
CORPORATE SOURCE: Department of Neurosurgery, Faculty of Medicine Paris-Sud, University of Paris XI, Bicetre, France..
songliu@club-internet.fr
SOURCE: NEUROSURGERY, (2001 Jul) 49 (1) 143-50; discussion 150-1.
Journal code: NZL; 7802914. ISSN: 0148-396X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200111
ENTRY DATE: Entered STN: 20011105
Last Updated on STN: 20011105
Entered Medline: 20011101

AB OBJECTIVE: A **collagen** tube was used to guide axonal regrowth from the spinal cord to the periphery to contribute to improvement of paralysis after lower thoracic spinal cord injury. METHODS: The spinal cords of adult male Sprague-Dawley rats were lesioned by removing the left hemicord from T12 to 5 mm below this level and additionally sectioning all left lumbar ventral roots. In experimental animals (n = 9), a **collagen** tube was inserted into this gap, spanning the rostral hemisected cord to the caudal sectioned lumbar ventral roots (gap, 7 mm). In control animals (n = 6), no treatment was performed. RESULTS: Six months after surgery, the return of some tension and resistance of the paralyzed hindlimb muscles was observed in all experimental rats except the untreated controls. Nine months postoperatively, muscle action potentials were recorded from the target muscles of the experimental animals while electrostimulating the tissue continuity within the **collagen** tube. Horseradish peroxidase retrograde labeling showed that the neurons in the rostral cord near the implantation site regrew into the reconnected lumbar ventral roots. Histological examination indicated numerous myelinated axons in the reconnected root pathways and newly formed endplates in the target muscles. No axonal regeneration was found in the control rats. CONCLUSION: These results indicate that the rostral spinal axons can regrow into the caudal sectioned and reconnected ventral roots through a **collagen** tube, thus innervating the denervated peripheral targets in adult rats after spinal cord injury. This surgical repair model also provides a means for testing the use of trophic factors that may further promote axonal regeneration.

L5 ANSWER 27 OF 69 MEDLINE
ACCESSION NUMBER: 2001268508 MEDLINE
DOCUMENT NUMBER: 21103044 PubMed ID: 11172368
TITLE: Bridging a peripheral nerve defect using **collagen** filaments.
AUTHOR: Yoshii S; Oka M; Ikeda N; Akagi M; Matsusue Y; Nakamura T
CORPORATE SOURCE: Department of Orthopaedic Surgery, Kansai Denryoku Hospital, Osaka, Japan.
SOURCE: JOURNAL OF HAND SURGERY. AMERICAN VOLUME, (2001 Jan) 26 (1) 52-9.
Journal code: IA9; 7609631. ISSN: 0363-5023.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20010709
Entered Medline: 20010705

AB We describe bridging a peripheral nerve defect using **collagen** filaments instead of a tube. Cords of **collagen** filaments were grafted to bridge 20-mm defects of rat sciatic nerves. Nerve autografts were grafted as the control. The mean number and the mean fiber diameter of regenerated myelinated axons were approximately 4,800 and 3.3 microm, respectively, in the distal end of the nerve autograft and approximately 5,500 and 2.3 microm, respectively, in the distal end of the **collagen**-filaments nerve guide 8 weeks after surgery. The mean number and the mean fiber diameter of regenerated myelinated axons were approximately 6,900 and 3.1 microm, respectively, in the distal end of the

nerve autograft and approximately 6,300 and 3.3 microm, respectively, in the distal end of the **collagen**-filaments nerve guide 25 weeks after surgery. Histologic studies suggested that the **collagen** filaments guided regenerating axons effectively. This new procedure offers a possible solution for the need to sacrifice a healthy nerve and for the shortage of graft material available for the repair of severed nerves.

L5 ANSWER 28 OF 69 MEDLINE
ACCESSION NUMBER: 2001133462 MEDLINE
DOCUMENT NUMBER: 21066570 PubMed ID: 11146062
TITLE: Peripheral **nerve regeneration** along **collagen** filaments.
AUTHOR: Yoshii S; Oka M
CORPORATE SOURCE: Institute of Biomedical Engineering, Kansai Denryoku Hospital, Imaichi 2-7-14, Asahi-ku, 535-0011, Osaka, Japan.. k-20433@kepco.co.jp
SOURCE: BRAIN RESEARCH, (2001 Jan 5) 888 (1) 158-162.
Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010301

AB This paper describes the regeneration of severed peripheral nerve axons along **collagen** filaments without a tube. Two thousand **collagen** filaments were grafted to bridge 20 mm defects of rat sciatic nerve. The number of myelinated axons was approximately 4800 in the distal end of the nerve autograft at 8 weeks postoperatively; while in the **collagen**-filaments nerve guide it was 5500. The results suggested the **collagen** filaments guided regenerating axons effectively.

L5 ANSWER 29 OF 69 MEDLINE
ACCESSION NUMBER: 2001038517 MEDLINE
DOCUMENT NUMBER: 20527574 PubMed ID: 11078137
TITLE: Facial nerve repair with expanded polytetrafluoroethylene and **collagen** conduits: an experimental study in the rabbit.
AUTHOR: Vasconcelos B C; Gay-Escoda C
CORPORATE SOURCE: University of Pernambuco Dental School, Recife, Brazil.
SOURCE: JOURNAL OF ORAL AND MAXILLOFACIAL SURGERY, (2000 Nov) 58 (11) 1257-62.
Journal code: JIC. ISSN: 0278-2391.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Dental Journals; Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001130

AB PURPOSE: This study evaluated autogenous nerve grafts and expanded polytetrafluoroethylene (e-PTFE) and **collagen** tubes as conduits for the repair of continuity defects in the facial nerve of rabbits. MATERIALS AND METHODS: The buccal division of 24 facial nerves was isolated, transected, and separated 10 mm. The gap between the 2 nerve ends was then repaired with an autologous nerve graft or an e-PTFE or **collagen** conduit. Fifteen days and 1, 2, and 4 months after the procedure, the animals were subjected to electrophysiologic tests, killed, and the nerves were removed for histologic examination. RESULTS: At 15 days postsurgery, no regeneration was observed through the e-PTFE and **collagen** tubes or across the autologous nerve grafts at the midpoint of the specimens. However, regeneration across the chambers and autologous nerve grafts was seen in the following 4 months, although the number of axons regenerated was small. CONCLUSIONS: The results of the

study indicate that e-PTFE and **collagen** tubing may be effective in the repair of continuity defects in peripheral nerves. However, further research will be necessary for generalization of this procedure.

L5 ANSWER 30 OF 69 MEDLINE
ACCESSION NUMBER: 2000492373 MEDLINE
DOCUMENT NUMBER: 20340235 PubMed ID: 10885726
TITLE: Peripheral **nerve regeneration** using silicone rubber chambers filled with **collagen**, laminin and fibronectin.
AUTHOR: Chen Y S; Hsieh C L; Tsai C C; Chen T H; Cheng W C; Hu C L; Yao C H
CORPORATE SOURCE: Institute of Chinese Medical Science, China Medical College, Taichung, Taiwan, ROC.
SOURCE: BIOMATERIALS, (2000 Aug) 21 (15) 1541-7.
Journal code: A4P; 8100316. ISSN: 0142-9612.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001027
Last Updated on STN: 20001027
Entered Medline: 20001013
AB A 10 mm gap of rat sciatic nerve was created between the proximal and distal nerve stumps, which were sutured into silicone rubber tubes filled with an extracellular gel containing **collagen**, laminin and fibronectin. Empty silicone rubber tubes were used as controls. Six weeks after implantation, all extracellular elements were completely degraded and absorbed, and 90% of the animals from the extracellular gel group exhibited regeneration across the nerve gaps, whereas only 60% in the control group. Both qualitative and quantitative histology of the regenerated nerves revealed a more mature ultrastructural organization with 28% larger cross-sectional area and 28% higher number of myelinated axons in the extracellular gel group than the controls. These results showed that the gel mixture of **collagen**, laminin and fibronectin could offer a suitable growth medium for the regeneration of axons.

L5 ANSWER 31 OF 69 MEDLINE
ACCESSION NUMBER: 2000434909 MEDLINE
DOCUMENT NUMBER: 20424537 PubMed ID: 10970120
TITLE: Peripheral **nerve regeneration** through bioresorbable and durable nerve guides.
AUTHOR: Navarro X; Rodriguez F J; Labrador R O; Buti M; Ceballos D; Gomez N; Cuadras J; Perego G
CORPORATE SOURCE: Departamento de Biologia Cel.lular i Fisiologia, Facultat de Medicina, Universitat Autonoma de Barcelona, Bellaterra, Spain.
SOURCE: JOURNAL OF THE PERIPHERAL NERVOUS SYSTEM, (1996) 1 (1) 53-64.
Journal code: C8N; 9704532. ISSN: 1085-9489.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000928
Last Updated on STN: 20000928
Entered Medline: 20000919
AB We compared reinnervation of target organs after sciatic nerve resection and repair by tubulization with biodurable tubes of silicone and teflon, or bioresorbable nerve guides of **collagen** and poly(L-lactide-co-6-caprolactone) (PLC) leaving a 6 mm gap in different groups of mice. All tubes were of 1 mm inside diameter and thin-walled (50 to 250 microm). Functional reinnervation was assessed by noninvasive methods to determine recovery of sweating, sensory and motor functions in the hindpaw repeatedly during 5 months postoperation. PLC guides allowed faster and higher levels of reinnervation for the four functions tested than **collagen** and silicone tubes, while teflon tubes gave the

lowest levels of recovery. Regenerative reinnervation by thin nociceptive and sudomotor fibers was higher than by large sensory and alphamotor fibers in all groups. Resorbable tubes promoted regeneration in a higher proportion of mice than durable tubes. In cases with effective regeneration the nerve cable was multifascicular, with mild to moderate mononuclear cell infiltrates and a thin newly formed perineurium. The number of myelinated fibers was higher in PLC and silicone tubes than in **collagen** and teflon tubes. There was only minimal inflammatory reaction within the remnants of **collagen** tubes, but not in the other materials. PLC tubes of slow reabsorption rate seem useful for repairing long gaps in injured nerves.

L5 ANSWER 32 OF 69 MEDLINE
ACCESSION NUMBER: 2000401895 MEDLINE
DOCUMENT NUMBER: 20314261 PubMed ID: 10854584
TITLE: Peripheral **nerve regeneration** across an 80-mm gap bridged by a polyglycolic acid (PGA)-**collagen** tube filled with laminin-coated **collagen** fibers: a histological and electrophysiological evaluation of regenerated nerves.
laminin collagen fibers

AUTHOR: Matsumoto K; Ohnishi K; Kiyotani T; Sekine T; Ueda H; Nakamura T; Endo K; Shimizu Y
CORPORATE SOURCE: Department of Bioartificial Organs, Institute for Frontier Medical Sciences, Kyoto University, Kawahara-cho 53, Shogoin Sakyo-ku, 606-8507, Kyoto, Japan.. matumoto@frontier.kyoto-u.ac.jp
SOURCE: BRAIN RESEARCH, (2000 Jun 23) 868 (2) 315-28. Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000901
Last Updated on STN: 20000901
Entered Medline: 20000818
AB We evaluated peripheral **nerve regeneration** across an 80-mm gap using a novel artificial nerve conduit. The conduit was made of a polyglycolic acid (PGA)-**collagen** tube filled with laminin-coated **collagen** fibers. Twelve beagle dogs underwent implantation of the nerve conduit across an 80-mm gap in the left peroneal nerve. In four other dogs used as negative controls, the nerve was resected and left unconnected. Histological observation showed that numerous unmyelinated and myelinated nerve fibers, all smaller in diameter and with a thinner myelin sheath than normal nerve fibers, regrew through and beyond the gap 12 months after implantation. The distribution of the regenerated axonal diameters was different from that of the normal axonal diameters. Compound muscle action potentials, motor evoked potentials, and somatosensory evoked potentials were recorded in most animals 3 months after implantation. Peak amplitudes and latencies recovered gradually, which indicating the functional establishment of the nerve connection with the target organs. In addition to the ordinary electrophysiological recoveries, potentials with distinct latencies originating from Aalpha, Adelta and C fibers became distinguishable at the 6th lumbar vertebra following stimulation of the peroneal nerve distal to the gap 12 months after implantation. The pattern of walking without load was restored to almost normal 10-12 months after implantation. Neither electrophysiological nor histological restoration was obtained in the controls. Our nerve conduit can guide peripheral nerve elongation and lead to favorable functional recovery across a wider nerve gap than previously reported artificial nerve conduits.

L5 ANSWER 33 OF 69 MEDLINE
ACCESSION NUMBER: 2000163799 MEDLINE
DOCUMENT NUMBER: 20163799 PubMed ID: 10701864
TITLE: Connective tissue response to tubular **implants** for peripheral **nerve regeneration**: the role of myofibroblasts.
AUTHOR: Chamberlain L J; Yannas I V; Hsu H P; Spector M

CORPORATE SOURCE: Department of Mechanical Engineering, Massachusetts Institute of Technology, Cambridge 02139, USA.
CONTRACT NUMBER: RO1 DE13053 (NIDCR)
SOURCE: JOURNAL OF COMPARATIVE NEUROLOGY, (2000 Feb 21) 417 (4) 415-30.
Journal code: HUV; 0406041. ISSN: 0021-9967.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000327
Last Updated on STN: 20000327
Entered Medline: 20000316

AB The presence of contractile cells, their organization around regenerating nerve trunks, and the hypothetical effect of these organized structures on the extent of regeneration across a tubulated 10-mm gap in the rat sciatic nerve were investigated. **Collagen** and silicone tubes were implanted both empty and filled with a **collagen** -glycosaminoglycan (GAG) matrix. Nerves were retrieved at 6, 30, and 60 weeks postoperatively and time-dependent values of the nerve trunk diameter along the tubulated length were recorded. The presence of myofibroblasts was identified immunohistochemically using a monoclonal antibody to alpha-smooth muscle actin. Myofibroblasts were circumferentially arranged around the perimeter of regenerated nerve trunks, forming a capsule which was about 10 times thicker in silicone tubes than in **collagen** tubes. The nerve trunk diameter that formed inside **collagen** tubes was twice as large as that inside silicone tubes. In contrast, the **collagen**-GAG matrix had a relatively small effect on capsule thickness or diameter of regenerate. It was hypothesized that the frequency of successful bridging by axons depends on the balance between two competitive forces: the axial forces generated by the outgrowth of axons and nonneuronal cells from the proximal stump and the constrictive, circumferential forces imposed by the contractile tissue capsule that promote closure of the wounded stumps and prevent axon elongation. Because the presence of the **collagen** -GAG matrix has enhanced greatly the recovery of normal function of regenerates in silicone tubes, it was hypothesized that it accelerated axonal elongation sufficiently before the hypothetical forces constricting the nerve trunk in silicone tubes became sufficiently large. The combined data suggest a new mechanism for peripheral **nerve** **regeneration** along a tubulated gap.

L5 ANSWER 34 OF 69 MEDLINE
ACCESSION NUMBER: 1999318254 MEDLINE
DOCUMENT NUMBER: 99318254 PubMed ID: 10391370
TITLE: Alpha-melanocyte stimulating hormone promotes regrowth of injured axons in the adult rat spinal cord.
AUTHOR: Joosten E A; Majewska B; Houweling D A; Bar P R; Gispen W H
CORPORATE SOURCE: Department of Neurology, Rudolf Magnus Institute for Neurosciences, University of Utrecht, The Netherlands..
e.a.s.joosten@neuro.azu.nl
SOURCE: JOURNAL OF NEUROTRAUMA, (1999 Jun) 16 (6) 543-53.
Journal code: J82; 8811626. ISSN: 0897-7151.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991123

AB Peptides related to melanotropin (alphaMSH) and corticotropin (ACTH), collectively termed melanocortins, are known to improve the postlesion repair of injured peripheral nerves. In addition, melanocortins exert trophic effects on the outgrowth of neurites from central nervous system neurons in vitro. Here we report, for the first time, the stimulation by alpha-MSH of spinal neurite outgrowth in vivo after injury. In the in vivo model, spinal cord trauma was produced at lower thoracic spinal levels of

adult rats. Under a surgical microscope a laminectomy was performed exposing the dorsum of the spinal cord. Then the dura was cut longitudinally and the dorsal columns were identified. Iridectomy scissors were used to transect the dorsal half of the spinal cord bilaterally, thereby completely lesioning the main corticospinal tract component. Then the lesion gap was immediately filled with a solid **collagen** matrix. Ingrowth of fibers was quantified using an advanced image analyser using a video image of sections transmitted by a camera. In the control situation virtually no ingrowth of sprouting injured fibers into the **collagen** implant in the lesion gap was seen. However, when the **collagen** matrix contained 10(-8) M alpha-MSH, a profound and significant stimulation of fiber ingrowth into the implant was observed (alpha-MSH, 21.5 +/- 2.9%; control, 1.4 +/- 0.6% p < 0.01). A small percentage of these ingrowing fibers was CGRP-immunoreactive (17.0 +/- 4%), whereas no serotonergic ingrowth was observed. Furthermore, we found that local application of alpha-MSH directs a substantial amount of lesioned anterogradely labelled corticospinal tract axons to regrow into the **collagen** implant (alpha-MSH, 15.2 +/- 5.2%; control, 0.5 +/- 0.3%, p < 0.01). The observed fiber ingrowth is not accompanied by an invasion of astroglial or reactive microglial cells into the implant. In conclusion, inclusion of alpha-MSH in the **collagen** implant stimulates the regrowth of injured axons in the adult rat spinal cord.

L5 ANSWER 35 OF 69 MEDLINE
ACCESSION NUMBER: 1999229701 MEDLINE
DOCUMENT NUMBER: 99229701 PubMed ID: 10214888
TITLE: Functional recovery following nerve injury and repair by silicon tubulization: comparison of laminin-fibronectin, dialyzed plasma, **collagen** gel, and phosphate buffered solution.
AUTHOR: Terris D J; Cheng E T; Utley D S; Tarn D M; Ho P R; Verity A N
CORPORATE SOURCE: Stanford University Medical Center, Division of Otolaryngology/Head and Neck Surgery, CA 94305-5328, USA.. dterris@stanford.edu
SOURCE: AURIS, NASUS, LARYNX, (1999 Apr) 26 (2) 117-22. Journal code: 9FZ; 7708170. ISSN: 0385-8146.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990806
Last Updated on STN: 19990806
Entered Medline: 19990728

AB PURPOSE: This study was designed to investigate the potential for enhancement of peripheral **nerve regeneration** by the manipulation of the neural microenvironment with laminin-fibronectin solution (LF), dialyzed plasma (DP), **collagen** gel (CG), or phosphate buffered saline (PBS) in a silicon tubulization repair model. METHOD: A rat sciatic nerve model of injury and repair was used to study the effects of exogenous matrix precursors (contained in LF or DP), CG or PBS on **nerve regeneration**. A total of 50 Sprague-Dawley rats underwent left sciatic nerve transection and repair by silicon tubulization. The silicon tubules were either left empty (E), or filled with solutions of LF, DP, CG, or PBS. Nerve function was assessed preoperatively and then postoperatively, every 10 days for 90 days using sciatic functional indexes (SFI). On postoperative day 90, the sciatic nerves were harvested for histologic analysis and the posterior compartment muscles of each animal were harvested and weighed. Molecular analysis for two proteins associated with neural regeneration was performed on the nerve segments. RESULTS: All five animal groups demonstrated equivalent functional recovery. Comparison of the rate of recovery and mean maximal recovery between each group revealed no statistically significant differences, with P-values ranging from 0.30 to 0.95. Posterior compartment muscle masses were similar in all groups except for LF, whose animals had muscle masses 8-9% lower than CG, PBS, or E (P < 0.05). CONCLUSION: Alteration of the regenerating neural microenvironment with exogenous matrix precursors (LF, DP), CG or PBS

failed to improve sciatic functional recovery after nerve transection and silicon tubulization in this model. From this study, we conclude that LF, DP, CG, and PBS do not enhance the rate or degree of recovery of peripheral nerve function across a narrow gap when nerves are repaired by silicon tubulization.

L5 ANSWER 36 OF 69 MEDLINE
ACCESSION NUMBER: 1998429006 MEDLINE
DOCUMENT NUMBER: 98429006 PubMed ID: 9758039
TITLE: Early peripheral nerve healing in **collagen** and silicone tube **implants**: myofibroblasts and the cellular response.
AUTHOR: Chamberlain L J; Yannas I V; Arrizabalaga A; Hsu H P; Norregaard T V; Spector M
CORPORATE SOURCE: Department of Mechanical Engineering, Massachusetts Institute of Technology, Cambridge 02139, USA.
SOURCE: BIOMATERIALS, (1998 Aug) 19 (15) 1393-403. Journal code: A4P; 8100316. ISSN: 0142-9612.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981208

AB Injuries to peripheral nerves innervating a limb cause paralysis, and can necessitate amputation. The inability of the nerves to regenerate spontaneously and the limitations of autograft procedures led to the development of treatments involving insertion of the nerve ends into prosthetic tubular devices. Previous work showed that 'entubulation' of the nerve ends in a silicone tube containing a specific porous, resorbable **collagen**-GAG (CG) copolymer, serving as an analog of extracellular matrix, improved regeneration compared to an empty silicone tube. However, long-term treatment with silicone tubes produced constriction that caused partial degradation of the regenerated axons; for this and other reasons, implementation of a nondegradable tube may require a second surgical procedure for removal. In this study the silicone tube was replaced with porous and non-porous **collagen** tubes in order to produce fully degradable devices. CG-filled **collagen** tubes and controls (CG-filled silicone tubes and empty **collagen** and silicone tubes) were implanted in a 10-mm gap in the rat sciatic nerve, with three rats in each group. The regeneration was evaluated after six weeks using light microscope images of cross sections of the nerve that were digitized and analyzed. Histograms of the diameters of the axons were generated and compared. The cellular response to the implanted biomaterials was assessed histologically, and immunohistochemistry was performed using an antibody to alpha-smooth muscle actin in order to determine the presence of myofibroblasts (contractile cells). Axonal regrowth was comparable in porous **collagen**, non-porous **collagen**, and silicone tubes filled with a CG matrix. These results support the implementation of a degradable **collagen** tube in place of a silicone device. Confirming earlier work, regeneration through the silicone and **collagen** tubes was enhanced by the CG copolymer, compared to empty tubes. A notable finding was a continuous layer of myofibroblasts on the surfaces of all of the six silicone tube prostheses, but on the inner surface of only one of six **collagen** tubes (Fisher's exact tests; $P < 0.01$). This is the first report of contractile capsules around silicone tubes, and supports the use of degradable **collagen** tubes in peripheral **nerve regeneration**. Macrophages were found bordering both the silicone and **collagen** tubes, and in the case of the **collagen** tubes, appeared to be participating in the regulation of the tubes.

L5 ANSWER 37 OF 69 MEDLINE
ACCESSION NUMBER: 1998417591 MEDLINE
DOCUMENT NUMBER: 98417591 PubMed ID: 9743566
TITLE: **Collagen** containing neurotrophin-3 (NT-3) attracts regrowing injured corticospinal axons in the adult

rat spinal cord and promotes partial functional recovery.

AUTHOR: Houweling D A; Lankhorst A J; Gispen W H; Bar P R; Joosten E A

CORPORATE SOURCE: Department of Neurology, Rudolf Magnus Institute for Neurosciences, Utrecht University, Utrecht, 3508 GA, The Netherlands.

SOURCE: EXPERIMENTAL NEUROLOGY, (1998 Sep) 153 (1) 49-59. Journal code: EQF; 0370712. ISSN: 0014-4886.

PUB. COUNTRY: United States

LANGUAGE: Journal; Article; (JOURNAL ARTICLE)

FILE SEGMENT: English

ENTRY MONTH: Priority Journals

ENTRY DATE: 199810

Entered STN: 19981029

Last Updated on STN: 20000303

Entered Medline: 19981019

AB During development, neurotrophic factors play an important role in the guidance and outgrowth of axons. Our working hypothesis is that neurotrophic factors involved in the development of axons of a particular CNS tract are among the most promising candidates for stimulating and directing the regrowth of fibers of this tract in the lesioned adult animal. The neurotrophin NT-3 is known to be involved in the target selection of outgrowing corticospinal tract (CST) fibers. We studied the capacity of locally applied NT-3 to stimulate and direct the regrowth of axons of the CST in the lesioned adult rat spinal cord. We also studied the effect of NT-3 application on the functional recovery of rats after spinal cord injury, using the gridwalk test. NT-3 was applied at the site of the lesion dissolved into rat tail **collagen** type I. Four weeks after spinal cord injury and **collagen** implantation, significantly more CST fibers had regrown into the **collagen** matrix containing NT-3 (22 +/- 6%, mean +/- SEM) than into the control **collagen** matrix without NT-3 (7 +/- 2%). No CST fibers grew into areas caudal to the **collagen** implant. Despite the absence of regrowth of corticospinal axons into host tissue caudal to the lesion area, functional recovery was observed in rats with NT-3 containing **collagen implants**.

L5 ANSWER 38 OF 69 MEDLINE

ACCESSION NUMBER: 1998374081 MEDLINE

DOCUMENT NUMBER: 98374081 PubMed ID: 9710307

TITLE: Implantation of **collagen** IV/poly(2-hydroxyethyl methacrylate) hydrogels containing Schwann cells into the lesioned rat optic tract.

AUTHOR: Plant G W; Chirila T V; Harvey A R

CORPORATE SOURCE: Department of Anatomy and Human Biology, The University of Western Australia, Perth, Australia.

SOURCE: CELL TRANSPLANTATION, (1998 Jul-Aug) 7 (4) 381-91. Journal code: B02; 9208854. ISSN: 0963-6897.

PUB. COUNTRY: United States

LANGUAGE: Journal; Article; (JOURNAL ARTICLE)

FILE SEGMENT: English

ENTRY MONTH: Priority Journals

ENTRY DATE: 199810

Entered STN: 19990106

Last Updated on STN: 19990106

Entered Medline: 19981028

AB Poly (2-hydroxyethylmethacrylate) (PolyHEMA) hydrogels, when combined with extracellular matrix molecules and infiltrated with cultured Schwann cells, have the capability to induce CNS axonal regrowth after injury. We have further investigated these PolyHEMA hydrogels and their potential to bridge CNS injury sites. **Collagen** IV-impregnated hydrogels containing Schwann cells were implanted into the lesioned optic tract in 14 rats. On examination 2-4 months later, there was good adherence between the **implants** and CNS tissue, and large numbers of viable Schwann cells (S100+, GFAP+, Laminin+, and LNGFR+) were seen within the hydrogel matrices. Immunohistochemical analysis showed that the **collagen** IV-impregnated PolyHEMA hydrogels preferentially supported the transplanted Schwann cells and not host glial cells such as astrocytes

Collagen IV

(GFAP+) or oligodendroglia (CAII+). Macrophages (ED1+) were also seen within the sponge structure. Eighty-three percent of the implanted hydrogels contained RT97+ axons within their trabecular networks. Regrowing axons were associated with the transplanted Schwann cells and not with the small number of infiltrating astrocytes. RT97+ axons were traced up to 510 microm from the nearest host neuropil. These axons were sometimes myelinated by the transplanted Schwann cells and expressed the peripheral myelin marker Po+. WGA/HRP-labeled retinal axons were seen within transplanted hydrogel sponges, with 40% of the cases growing for distances up to 350-450 microm within the polymer network. The data indicate that impregnating PolyHEMA sponges with **collagen** IV can modify the host glial reaction and support the survival of transplanted Schwann cells. This study thus provides new information on how biomaterials could be used to modify and bridge CNS injury sites.

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L5 ANSWER 39 OF 69 MEDLINE
ACCESSION NUMBER: 1998204647 MEDLINE
DOCUMENT NUMBER: 98204647 PubMed ID: 9545086
TITLE: Axonal regrowth through a **collagen** guidance channel bridging spinal cord to the avulsed C6 roots: functional recovery in primates with brachial plexus injury.
AUTHOR: Liu S; Bodjarian N; Langlois O; Bonnard A S; Boisset N; Peulve P; Said G; Tadie M
CORPORATE SOURCE: Department of Neurosurgery, Hospital of Bicetre, Le Kremlin-Bicetre, France.
SOURCE: JOURNAL OF NEUROSCIENCE RESEARCH, (1998 Mar 15) 51 (6) 723-34.
Journal code: KAC; 7600111. ISSN: 0360-4012.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980708
Last Updated on STN: 19990129
Entered Medline: 19980622

AB Intraspinal implantation of a **collagen** guidance channel (CGC) to promote axon regeneration was investigated in marmosets with brachial plexus injury. After avulsion of the right C5, C6 and C7 spinal roots, a CGC containing (group B) or not (group A) a nerve segment, or a nerve graft (group C), was ventro-laterally implanted into the cord to bridge the ventral horn and the avulsed C6 roots. No spinal cord dysfunction was observed following surgery. Two months later, the postoperative flaccid paralysis of the lesioned arm improved. In five months, a normal electromyogram of the affected biceps muscle was recorded in all repaired animals. Motor evoked potentials were obtained with a mean amplitude of 13.37 +/- 13.66 microV in group A, 13.21 +/- 5.16 microV in group B and 37.14 +/- 35.16 microV in group C. The force of biceps muscle contraction was 27.33 +/- 20.03 g (group A), 24.33 +/- 17.03 g (group B) and 37.38 +/- 21.70 g (group C). Retrograde tracing by horseradish peroxidase showed labelled motoneurons ipsilaterally located in the C5 and C6 ventral horn, nearby the implantation site. The mean labelled neurons was 32.33 +/- 21.13, 219.33 +/- 176.29 and 64.33 +/- 23.54 in group A, B and C respectively. Histological analysis presented numerous myelinated and unmyelinated regenerating axons in the implant of these animals. Statistical analysis did not show significant difference among the three repaired groups. Our results indicate that spinal neurons can regenerate through a CGC to avulsed nerve roots and induce motor recovery in primates.

L5 ANSWER 40 OF 69 MEDLINE
ACCESSION NUMBER: 97429881 MEDLINE
DOCUMENT NUMBER: 97429881 PubMed ID: 9285519
TITLE: Axonal regrowth through **collagen** tubes bridging the spinal cord to nerve roots.
AUTHOR: Liu S; Peulve P; Jin O; Boisset N; Tiollier J; Said G; Tadie M
CORPORATE SOURCE: Department of Neurosurgery, Hospital of Bicetre, Le Kremlin

Bicetre, France.
SOURCE: JOURNAL OF NEUROSCIENCE RESEARCH, (1997 Aug 15) 49 (4) 425-32.
Journal code: KAC; 7600111. ISSN: 0360-4012.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971105
Last Updated on STN: 19980206
Entered Medline: 19971023

AB The capacity of central nervous system (CNS) axons to elongate from the spinal cord to the periphery throughout a tubular implant joining the ventral horn of the spinal cord to an avulsed root was investigated in a model of brachial plexus injury. The C5-C7 roots were avulsed by controlled traction and the C6 root was bridged to the spinal cord over a 3 mm gap by the use of a **collagen** cylinder containing or not containing an autologous nerve segment, or an autologous nerve graft. Nine months later, the functionality and the quality of the axonal regrowth was evaluated by electrophysiology, retrograde labelling of neurons, and histological examination of the gap area. A normal electromyogram of the biceps was observed in all animals where the C6 root was bridged to the spinal cord. The mean average amplitude of the motor evoked potentials was comprised between 17.51 +/- 12.03 microV in animals repaired with a **collagen** cylinder, and 27.83 +/- 22.62 microV when a nerve segment was introduced in the tube. In nonrepaired animals spontaneous potentials reflecting a muscle denervation were observed at electromyography. Retrograde labelling indicated that a mean number of 58.88 +/- 37.89 spinal cord neurons have reinnervated the biceps in animals repaired with a tube versus 78.38 +/- 62.11 when a nerve segment was introduced in the channel, and 97.25 +/- 56.23 in nerve grafting experiments. Analyses of the repair site showed the presence of numerous myelinated regenerating axons. In conclusion, our results indicate that spinal cord neurons can regenerate through tubular **implants** over a 3 mm gap, and that this axonal regrowth appeared as effective as in nerve grafting experiments. The combination of an implant and a nerve segment did not significantly increase the regeneration rate.

L5 ANSWER 41 OF 69 MEDLINE
ACCESSION NUMBER: 96349812 MEDLINE
DOCUMENT NUMBER: 96349812 PubMed ID: 8741371
TITLE: Peripheral **nerve regeneration** in a silicone tube: effect of **collagen** sponge prosthesis, laminin, and pyrimidine compound administration.
AUTHOR: Ohbayashi K; Inoue H K; Awaya A; Kobayashi S; Kohga H; Nakamura M; Ohye C
CORPORATE SOURCE: Department of Neurosurgery, Gunma University School of Medicine, Maebashi.
SOURCE: NEUROLOGIA MEDICO-CHIRURGICA, (1996 Jul) 36 (7) 428-33.
Journal code: NYD; 0400775. ISSN: 0470-8105.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961106
Last Updated on STN: 19980206
Entered Medline: 19961023

AB Regeneration of transected peripheral nerve with a 10-mm gap encased in a silicone tube was evaluated in the presence of **collagen** sponge with or without laminin, or with systemic administration of a pyrimidine compound, MS-818. The sciatic nerve of 20 adult rats was transected and the proximal and distal nerve stumps were fixed in a silicone tube. The lumen of the silicone tube was empty, or filled with a **collagen** sponge alone or with a laminin-soaked **collagen** sponge. Also, a pyrimidine compound was injected intraperitoneally after implantation of the empty silicone tube. Three weeks later, the contents of the silicone

tubes were processed for histological examination of regenerated nerve fibers. Other animals were observed 6, 12, and 18 months after surgery to examine the long-term effects of the **collagen** sponge on **nerve regeneration**. All animals had regenerated tissue within the tube 3 weeks after nerve transection. The diameter of the tissue decreased toward the distal stump in the empty tube, but was the same throughout the full length in the **collagen** sponge-containing tube. Immunohistochemical studies revealed that the nerve fibers extended beyond the midline of the regenerated tissue in animals treated with a laminin-containing **collagen** sponge or receiving a pyrimidine compound. Long-term observation showed the regenerated nerve was thick as the proximal stump and many neurofilament- and peripheral myelin-positive fibers were observed around the **collagen** sponge. **Collagen** sponge assists the progress of regenerated tissues in silicone tubes, and laminin-containing prostheses and administration of a pyrimidine compound enhance peripheral **nerve regeneration**.

filling
related

L5 ANSWER 42 OF 69 MEDLINE
ACCESSION NUMBER: 96059014 MEDLINE
DOCUMENT NUMBER: 96059014 PubMed ID: 7473879
TITLE: **Collagen implants** and cortico-spinal axonal growth after mid-thoracic spinal cord lesion in the adult rat.
AUTHOR: Joosten E A; Bar P R; Gispen W H
CORPORATE SOURCE: Department of Neurology, Rudolf Magnus Institute for Neurosciences, University of Utrecht, The Netherlands.
SOURCE: JOURNAL OF NEUROSCIENCE RESEARCH, (1995 Jul 1) 41 (4) 481-90.
Journal code: KAC; 7600111. ISSN: 0360-4012.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19960124
Entered Medline: 19951124

AB We describe an experimental model to study regeneration of lesioned corticospinal tract (CST) fibers in the adult rat spinal cord. After transection of all CST fibers at mid-thoracic level the gap is grafted with a sterile, cell-free **collagen** matrix. Two methods of **collagen**-application are used: 1) injection of a fluid **collagen** solution into the lesioned area which self-assembles in situ and 2) implantation of a solid **collagen** gel. At 4 weeks post-implantation CST axons are anterogradely labelled with horseradish-peroxidase (HRP). The **collagen** implant is evaluated for ingrowth of CST axons. The histopathological reaction (gliotic response) around the lesion and within the matrix is also studied. After application of a fluid **collagen** solution into the lesion area HRP-labelled CST axons can be visualized within the implant. In addition, astroglial and reactive microglial cells invade the **collagen** -matrix. On the other hand, if **collagen** is implanted as an already self-assembled gel, no ingrowth of labelled CST axons nor of astroglial/reactive microglial cells is observed. Both methods of **collagen**-application result in a considerable reduction of the gliotic response as compared to the ungrafted animals. We conclude that the method of application of **collagen** (i.e., fluid or gel) considerably affects the response of lesioned CST axons. The application of a fluid **collagen** graft which in situ self-assembles is beneficial for the regrowth of lesioned CST axons in rat spinal cord. In this respect the formation of an astroglial scaffolding structure within the (fluid) **collagen**, probably due to optimal integration between host and graft, is very important. The inability of injured CST fibers to enter the solid **collagen** graft may be related to the absence of an astroglial scaffolding structure within the implant.

L5 ANSWER 43 OF 69 MEDLINE
ACCESSION NUMBER: 95245754 MEDLINE

DOCUMENT NUMBER: 95245754 PubMed ID: 7728523
TITLE: Axonal growth within poly (2-hydroxyethyl methacrylate) sponges infiltrated with Schwann cells and implanted into the lesioned rat optic tract.
AUTHOR: Plant G W; Harvey A R; Chirila T V
CORPORATE SOURCE: Department of Anatomy and Human Biology, University of Western Australia, Nedlands, Perth.
SOURCE: BRAIN RESEARCH, (1995 Feb 6) 671 (1) 119-30.
Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950608
Last Updated on STN: 19950608
Entered Medline: 19950601

AB Porous hydrophilic sponges made from 2-hydroxyethyl methacrylate (HEMA) have a number of possible biomedical applications. We have investigated whether these poly(HEMA) hydrogels, when coated with **collagen** and infiltrated in vitro with cultured Schwann cells, can be implanted into the lesioned optic tract and act as prosthetic bridges to promote axonal regeneration. Nineteen rats (20-21 days old) were given hydrogel/Schwann cell **implants**. No obvious toxic effects were seen, either to the transplanted glia or in the adjacent host tissue. Schwann cells survived the implantation technique and were immunopositive for the low affinity nerve growth factor receptor, S100 and laminin. Immunohistochemical studies showed that host non-neuronal cells (astrocytes, oligodendroglia and macrophages) migrated into the implanted hydrogels. Astrocytes were the most frequently observed host cell in the polymer bridges. RT97-positive axons were seen in about two thirds of the **implants**. The axons were closely associated with transplanted Schwann cells and, in some cases, host glia (astrocytes). Individual axons regrowing within the implanted hydrogels could be traced for up to 900 microns, showing that there was continuity in the network of channels within the polymer scaffold. Axons did not appear to be myelinated by either Schwann cells or by migrated host oligodendroglia. In three rats, anterograde tracing with WGA/HRP failed to demonstrate the presence of retinal axons within the hydrogels. The data indicate that poly(HEMA) hydrogels containing Schwann cells have the potential to provide a stable three-dimensional scaffold which is capable of supporting axonal regeneration in the damaged CNS.

L5 ANSWER 44 OF 69 MEDLINE
ACCESSION NUMBER: 95213755 MEDLINE
DOCUMENT NUMBER: 95213755 PubMed ID: 7699407
TITLE: Transplantation of purified populations of Schwann cells into lesioned adult rat spinal cord.
AUTHOR: Bunge M B
CORPORATE SOURCE: Miami Project to Cure Paralysis, University of Miami School of Medicine, Florida.
CONTRACT NUMBER: 09923 (NINDS)
NS28059
SOURCE: JOURNAL OF NEUROLOGY, (1994 Dec) 242 (1 Suppl 1) S36-9.
Ref: 12
Journal code: JB7; 0423161. ISSN: 0340-5354.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 19950510
Last Updated on STN: 19980206
Entered Medline: 19950503

AB Both peripheral nerve and purified populations of Schwann cells promote axonal regeneration in the peripheral and central nervous systems. In order to assess whether Schwann cells can provide a bridge enabling

regrowth of descending and ascending axons across an area of injury in adult spinal cord, Schwann cells enclosed within a **collagen** scroll were transplanted into lesions created photochemically. Numerous myelinated and unmyelinated axons were found throughout 28-90 day **implants**; Schwann cells myelinated or ensheathed the ingrowing axons normally. In contrast, acellular **collagen** grafts did not contain axons. Thus, Schwann cells stimulated abundant growth of axons into the grafts. In part to address the concern that the dense **collagen** layer acted as a barrier, we assessed transplantation of Schwann cells, inside semipermeable polyacrylonitrile/polyvinylcholoride (PAN/PVC) guidance channels, after transection of adult inbred rat spinal cords at T8 with removal of the the T9-11 segments. One month after grafting, a vascularized tissue cable was present with more myelinated and unmyelinated axons in the Schwann cell seeded channels than controls. (ABSTRACT TRUNCATED AT 250 WORDS)

L5 ANSWER 45 OF 69 MEDLINE
ACCESSION NUMBER: 95153321 MEDLINE
DOCUMENT NUMBER: 95153321 PubMed ID: 7850464
TITLE: Sciatic **nerve regeneration** navigated by laminin-fibronectin double coated biodegradable **collagen** grafts in rats.
AUTHOR: Tong X J; Hirai K; Shimada H; Mizutani Y; Izumi T; Toda N; Yu P
CORPORATE SOURCE: Department of Anatomy, Kanazawa Medical University, Ishikawa, Japan.
SOURCE: BRAIN RESEARCH, (1994 Nov 7) 663 (1) 155-62. Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: English
ENTRY MONTH: Priority Journals
ENTRY DATE: 199503
Entered STN: 19950322
Last Updated on STN: 19950322
Entered Medline: 19950314

laminin fibron

type I collagen Tch

AB Biodegradable type I **collagen** tube grafts filled longitudinally with laminin and fibronectin double coated **collagen** fiber bundles (L-F grafts) were implanted to promote sciatic **nerve regeneration** in rats. Grafts filled with uncoated **collagen** fibers were used as control. A 1 cm defect on the right sciatic nerve was filled with a graft in the manner of bridging. Thirty days after implantation, several newly developed nerve fasciculi were found at the middle portion of the L-F grafts in contrast to no developed nerves in the controls. After 60 days, the middle and distal portions of both grafts included well-developed nerve tissues with prominent myelinated and unmyelinated nerve fibers surrounded by perineural cells, but the control distal portion showed fewer nerve fibers. All artificial **collagen** elements were completely degraded and absorbed at 30 days, and new nerve tissues surrounded by an epineurium successfully connected the proximal stump to the distal stump of the initially separated nerve. Descending and ascending action potentials were evoked in all grafts at 60 days. These results indicated that laminin and fibronectin may promote the growth of axons in biodegradable **collagen** grafts, which guided **nerve regeneration** well and allowed the formation of epineurium.

L5 ANSWER 46 OF 69 MEDLINE
ACCESSION NUMBER: 95054214 MEDLINE
DOCUMENT NUMBER: 95054214 PubMed ID: 7964912
TITLE: Regrowth of axons in lesioned adult rat spinal cord: promotion by **implants** of cultured Schwann cells.
AUTHOR: Paino C L; Fernandez-Valle C; Bates M L; Bunge M B
CORPORATE SOURCE: Chambers Family Electron Microscopy Laboratory, University of Miami School of Medicine FL 33136.
CONTRACT NUMBER: NS09923 (NINDS)
NS28059 (NINDS)
SOURCE: JOURNAL OF NEUROCYTOLOGY, (1994 Jul) 23 (7) 433-52. Journal code: JB3; 0364620. ISSN: 0300-4864.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941208

AB Highly purified populations of Schwann cells were grafted into lesioned adult rat spinal cord to determine if they promote axonal regeneration. Dorsal spinal cord lesions were created by a photochemical lesioning technique. Schwann cells derived from E16 rat dorsal root ganglia, either elongated and associated with their extracellular matrix or dissociated and without matrix, were rolled in polymerized **collagen** to form an implant 4-6 mm long which was grafted at 5 or 28 days after lesioning. No immunosuppression was used. Acellular **collagen** rolls served as controls. At 14, 28 and 90 days and 4 and 6 months after grafting, animals were analysed histologically with silver and Toluidine Blue stains and EM. The grafts often filled the lesion and the host borders they apposed exhibited only limited astrogliosis. By 14 days, bundles of unmyelinated and occasional thinly myelinated axons populated the periphery of Schwann cell **implants**. By 28 days and thereafter, numerous unmyelinated and myelinated axons were present in most grafts. Silver staining revealed sprouted axons at the implant border at 28 days and long bundles of axons within the implant at 90 days. Photographs of entire 1 micron plastic cross-sections of nine grafted areas were assembled into montages to count the number of myelinated axons at the graft midpoint; the number of myelinated axons ranged from 517-3214. Electron microscopy of **implants** showed typical Schwann cell ensheathment and myelination, increased myelin thickness by 90 days, and a preponderance of unmyelinated over myelinated axons. Random EM sampling of five Schwann cell grafts showed that the ratio of unmyelinated to myelinated axons was highest (20:1) at 28 days. These ratios implied that axons numbered in the thousands at the graft midpoint. Dissociated Schwann cells without matrix promoted axonal ingrowth and longitudinal orientation as effectively as did elongated Schwann cells accompanied by matrix. There was a suggestion that axonal ingrowth was at least as successful, if not more so, when the delay between lesioning and grafting was 28 rather than 5 days. Acellular **collagen** grafts did not contain axons at 28 days, the only interval assessed. In sum, grafts of Schwann cells in a rolled **collagen** layer filled the lesion and were well tolerated by the host. The Schwann cells stimulated rapid and abundant growth of axons into grafts and they ensheathed and myelinated these axons in the normal manner.

L5 ANSWER 47 OF 69 MEDLINE
ACCESSION NUMBER: 94133209 MEDLINE
DOCUMENT NUMBER: 94133209 PubMed ID: 8301633
TITLE: Peripheral **nerve regeneration** across 14-mm gaps: a comparison of autograft and entubulation repair methods in the rat.
AUTHOR: Keeley R; Atagi T; Sabelman E; Padilla J; Kadlcik S; Keeley A; Nguyen K; Rosen J
CORPORATE SOURCE: Department of Functional Restoration, Stanford University Medical School, California.
SOURCE: JOURNAL OF RECONSTRUCTIVE MICROSURGERY, (1993 Sep) 9 (5) 349-58; discussion 359-60.
Journal code: JVX; 8502670. ISSN: 0743-684X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940318
Last Updated on STN: 19980206
Entered Medline: 19940307

AB A study was conducted to compare the regeneration across 1.4-cm peroneal nerve gaps in rats, repaired with sutured autografts or with artificial nerve grafts. The artificial models were composed of a biodegradable

passive conduit made of glycolide trimethylene carbonate, filled with either phosphate-buffered saline or a **collagen** extracellular matrix. Functional recovery was evaluated by walking track analysis throughout the experiment. After 9 months, the nerves were analyzed by electrophysiology and by qualitative and quantitative histology. Walking track analysis demonstrated the three repair methods to provide statistically equivalent recovery, except at day 195 post-engraftment, when the **collagen**-filled conduit was superior to the saline-filled conduit. Electrophysiologically, the autograft was superior to the **collagen**-filled conduit, while the **collagen**- and saline-filled conduits were equivalent. Quantitative histology demonstrated that normal intact nerve had larger mean myelinated axonal diameters but an equal number of axons to the three repair methods, and that the repair methods were statistically equivalent. While the repair methods had similar histologic and functional outcomes, combined standardized scoring demonstrated that the autograft was superior to the statistically-equivalent entubulation repairs. A **collagen** gel may serve as an ideal matrix in which to suspend neurotrop(h)ic factors or cells.

L5 ANSWER 48 OF 69 MEDLINE
ACCESSION NUMBER: 94133208 MEDLINE
DOCUMENT NUMBER: 94133208 PubMed ID: 8301632
TITLE: Sciatic **nerve regeneration** across gaps within **collagen** chambers: the influence of epidermal growth factor.
AUTHOR: Dubuisson A S; Beuermann R W; Kline D G
CORPORATE SOURCE: Department of Neurosurgery, Louisiana State University Medical Center, New Orleans.
SOURCE: JOURNAL OF RECONSTRUCTIVE MICROSURGERY, (1993 Sep) 9 (5) 341-6; discussion 346-7.
Journal code: JVX; 8502670. ISSN: 0743-684X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940318
Last Updated on STN: 20000303
Entered Medline: 19940307
AB The effects of Epidermal Growth Factor (EGF) on axonal regeneration of a sectioned sciatic nerve within **collagen** tubes were investigated in 15 rats. Following baseline electrophysiologic assessment, bilateral 7-mm nerve gaps were created and repaired by interposition of **collagen** tubes, into which EGF (left side) or type I **collagen** (right side) was instilled. After 4 or 8 weeks, axonal regeneration, measured by electrophysiologic and histologic means, was identical for the EGF and control legs. The conclusion is that EGF does not influence **nerve regeneration** within a **collagen** chamber.

L5 ANSWER 49 OF 69 MEDLINE
ACCESSION NUMBER: 94111079 MEDLINE
DOCUMENT NUMBER: 94111079 PubMed ID: 8283421
TITLE: Comparison of macropore, semipermeable, and nonpermeable **collagen** conduits in nerve repair.
AUTHOR: Kim D H; Connolly S E; Zhao S; Beuerman R W; Voorhies R M; Kline D G
CORPORATE SOURCE: Department of Neurosurgery, Louisiana State University Medical Center, New Orleans 70112.
SOURCE: JOURNAL OF RECONSTRUCTIVE MICROSURGERY, (1993 Nov) 9 (6) 415-20.
Journal code: JVX; 8502670. ISSN: 0743-684X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199402
ENTRY DATE: Entered STN: 19940228

Last Updated on STN: 19980206
Entered Medline: 19940216

AB Twelve rabbits were used to study functional **nerve regeneration** through macropore, semipermeable, and nonpermeable **collagen** conduits. Each animal underwent a 10-mm bilateral resection of posterior tibial nerve. Lesions were repaired with a macropore **collagen** tube in one leg, and with a semipermeable or a nonpermeable **collagen** tube contralaterally. Functional **nerve regeneration** was evaluated at 6 and 12 weeks post-repair periods. Functional recovery was assessed by electrophysiologic analysis of nerve conduction velocity, amplitude of nerve action potential, amplitude and area of muscle action potential, and by quantitative and qualitative histologic analysis of myelinated nerve fibers from the distal nerve stumps. The macropore-**collagen**-tube group showed significantly greater functional recoveries than semipermeable or nonpermeable **collagen**-tube groups, based on electrophysiologic and histologic analyses.

L5 ANSWER 50 OF 69 MEDLINE
ACCESSION NUMBER: 94110894 MEDLINE
DOCUMENT NUMBER: 94110894 PubMed ID: 8283264
TITLE: Labeled Schwann cell transplants versus sural nerve grafts in nerve repair.
AUTHOR: Kim D H; Connolly S E; Kline D G; Voorhies R M; Smith A; Powell M; Yoes T; Daniloff J K
CORPORATE SOURCE: Department of Neurosurgery, Louisiana State University Medical Center, New Orleans.
SOURCE: JOURNAL OF NEUROSURGERY, (1994 Feb) 80 (2) 254-60.
Journal code: JD3; 0253357. ISSN: 0022-3085.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199402
ENTRY DATE: Entered STN: 19940228
Last Updated on STN: 19940228
Entered Medline: 19940217

AB This study evaluated the ability of Schwann cell transplants to enhance the recovery of function in injured nerves and compared the results to those produced by sural nerve grafts. Schwann cells were isolated from sciatic nerves, prelabeled with gold fluorescent dye admixed with **collagen** gel, and placed in resorbable **collagen** tubes. Twenty-four adult rats underwent severing of the bilateral sciatic nerves, with a 10-mm gap between the nerve stumps. The rats were then divided into two groups. A **collagen** tube with implanted Schwann cells was implanted in one leg of the Group I rats, and the contralateral leg served as a control and was repaired with a **collagen** tube filled with **collagen** gel only. The Group II animals received conduits packed with labeled Schwann cells in one leg to bridge the 10-mm gap; the contralateral leg was repaired with an autogenous sural nerve graft. Recovery of function was assessed physiologically and morphologically. Nerve conduction velocity and nerve action potential amplitude measurements showed that the Schwann cell **implants** induced return of function comparable to that of the sural nerve grafts. Morphological assessments of myelination suggested a tendency toward greater numbers of myelinated axons in Schwann cell **implants** than in sural nerve grafts. Anatomical analyses of gold fluorescent dye showed both high viability of prelabeled Schwann cells at 120 days after transplantation and migration as far as 30 mm away from the implant site.

L5 ANSWER 51 OF 69 MEDLINE
ACCESSION NUMBER: 93208617 MEDLINE
DOCUMENT NUMBER: 93208617 PubMed ID: 8457891
TITLE: Evaluation of two cross-linked **collagen** gels implanted in the transected spinal cord.
AUTHOR: Marchand R; Woerly S; Bertrand L; Valdes N
CORPORATE SOURCE: Centre de Recherche en Neurobiologie, Hopital de l'Enfant-Jesus, Quebec, Canada.
SOURCE: BRAIN RESEARCH BULLETIN, (1993) 30 (3-4) 415-22.

Journal code: B5M; 7605818. ISSN: 0361-9230.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 19930514
Last Updated on STN: 19980206
Entered Medline: 19930427

AB In previous experiments, we have shown that spinal axons grow into a **collagen** matrix implanted between the stumps of a transected spinal cord. However, the matrix became denatured after 2 to 3 months. To improve the stability and the durability of the **collagen** gel **implants**, **collagen** was coprecipitated with chondroitin-6-sulfate (C-6-S) or chemically cross-linked with carbodiimide (CD). The spinal cords were taken out after 3 days, 1, 3, or 6 months and analyzed using different histological and tracing techniques. The cross-linked **collagen** matrices underwent major structural changes. Cross-linking treatments improved the stability of **collagen implants** which withstood at least 6 months. Axons revealed with DiI or silver staining crossed the proximal interface and grew into the bioimplants. Some axons were also followed across the distal bioimplant-spinal interface in DiI treated tissues. This study suggests that cross-linking the **collagen** hydrogel has improved the mechanical properties of the matrix, modified the normal scarring process, and favored axonal regeneration.

L5 ANSWER 52 OF 69 MEDLINE
ACCESSION NUMBER: 93050025 MEDLINE
DOCUMENT NUMBER: 93050025 PubMed ID: 1426123
TITLE: Regeneration of dorsal root axons is related to specific non-neuronal cells lining NGF-treated intraspinal nitrocellulose **implants**.
AUTHOR: Houle J D
CORPORATE SOURCE: Department of Anatomy, University of Arkansas for Medical Sciences, Little Rock 72205.
CONTRACT NUMBER: NS 26380 (NINDS)
SOURCE: EXPERIMENTAL NEUROLOGY, (1992 Nov) 118 (2) 133-42.
Journal code: EQF; 0370712. ISSN: 0014-4886.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19980206
Entered Medline: 19921222

NGF

AB The regeneration of sensory axons from severed dorsal roots can be enhanced by the presence of nerve growth factor (NGF)-treated nitrocellulose strips implanted into an intraspinal lesion cavity. Rather than being directly apposed to the transplant, most regenerating axons are separated from the nitrocellulose by several layers of non-neuronal cells, suggesting that these cells may have a role in the promotion of axonal regrowth. The cellular layers associated with untreated nitrocellulose strips or NGF-treated **implants** were examined in this study to determine if there were differences in their arrangement or orientation along the implant which might explain some of the possible effects of substrate-bound NGF on axonal regrowth. Into a hemisection lesion cavity created in the adult rat lumbar spinal cord NGF-treated or untreated strips of nitrocellulose were placed vertically, with intact pieces of fetal spinal cord (FSC) tissue transplanted along each side. The distal ends of cut dorsal rootlets were apposed to the fetal tissue. Immunocytochemical and electron microscopic examination 30-60 days post-transplantation revealed a distinct layering of cell types along the NGF-treated strips. Closest to the nitrocellulose was a single layer of macrophages, followed by a separate layer of fibroblasts with dense **collagen** bundles, then a layer of astroglial cells, before reaching the neuropil of the fetal spinal cord tissue. A thickened basal lamina formed between the fibroblast and astrocytic cell layers and

bundles of regenerated sensory axons extended along the interface between these two layers. In contrast, non-neuronal cells along untreated nitrocellulose strips were not as well organized, with an intermixing of fibroblasts and astroglial cells and only scattered macrophage-like cells. Axons rarely were found in conjunction with this mixed population of cells and, overall, fewer regenerated axons extended into transplants with untreated nitrocellulose. The results demonstrate consistent differences in the composition and organization of non-neuronal cells adjacent to NGF-treated nitrocellulose **implants**, compared to untreated **implants**. This suggests that the presence of bound NGF influences the recruitment of various cells from the surrounding transplant tissue as well as from the previously injured dorsal rootlets. The capacity for NGF to promote the regeneration of sensory axons may be an indirect effect that is mediated or potentiated by the non-neuronal cell population that gathers in response to the presence of bound NGF.

L5 ANSWER 53 OF 69 MEDLINE
ACCESSION NUMBER: 92251670 MEDLINE
DOCUMENT NUMBER: 92251670 PubMed ID: 1315866
TITLE: Artificial nerve graft using glycolide trimethylene carbonate as a nerve conduit filled with **collagen** compared to sutured autograft in a rat model.
AUTHOR: Rosen J M; Padilla J A; Nguyen K D; Siedman J; Pham H N
CORPORATE SOURCE: Division of Plastic and Reconstructive Surgery, Stanford University Medical Center, Palo Alto, CA 94305.
SOURCE: JOURNAL OF REHABILITATION RESEARCH AND DEVELOPMENT, (1992 Spring) 29 (2) 1-12.
Journal code: JRD; 8410047. ISSN: 0748-7711.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920619
Last Updated on STN: 19980206
Entered Medline: 19920611
AB A study was conducted to compare the regeneration of rat peroneal nerves across 0.5 cm gaps repaired with artificial nerve grafts (ANG) versus sutured autografts (SAG). The ANG model is composed of a synthetic biodegradable passive conduit made of glycolide trimethylene carbonate (GTMC) filled with a **collagen** matrix (predominantly Type I **collagen**, derived from calf skin, and with the telopeptide ends left intact). Axonal regeneration was studied in 11 long-term animals (two at 6 months and nine at 9 months). The nerves were studied by qualitative and quantitative histological, electrophysiological, and functional assays. Axonal regeneration with the ANG was equal to SAGs as measured by axonal diameters, physiological, and functional methods, although the SAG demonstrated statistically higher axonal counts.

L5 ANSWER 54 OF 69 MEDLINE
ACCESSION NUMBER: 92239506 MEDLINE
DOCUMENT NUMBER: 92239506 PubMed ID: 1571396
TITLE: Intracerebral implantation of ionic synthetic hydrogels: effect of polar substrata on astrocytosis and axons.
AUTHOR: Woerly S; Lavallee C; Marchand R
CORPORATE SOURCE: Centre de recherche en neurobiologie, Hopital de l'Enfant Jesus, Universite Laval, Quebec, Canada.
SOURCE: JOURNAL OF NEURAL TRANSPLANTATION AND PLASTICITY, (1992 Jan-Mar) 3 (1) 21-34.
Journal code: A2A; 9104161. ISSN: 0792-8483.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920619
Last Updated on STN: 19970203
Entered Medline: 19920604
AB In previous studies, hyperporous synthetic hydrogels of poly(glyceryl

methacrylate) or p(GMA), containing bioadhesive substrates of **collagen**, were implanted into rat cerebral tissue in order to provide systems of oriented guidance channels for directing the growth of the scar and axons /28/. In the present study, ionic p(GMA)-**collagen** hydrogels containing polar chemical groups, either basic amino groups or acidic carboxyl groups, were evaluated for their tolerance and their effects on the brain scarring response and axonal reactivity after long-term implantation in the cerebral cortex. In all animals, the **implants** were well tolerated. Although both types of gels influenced the astroglial reaction near the bioimplant, hydrogels carrying carboxyl groups had the strongest influence on the elongation, the direction and the organization of astrocytic processes so that a glial matrix could form in regions of the gel. Extracellular material (e.g. reticulin) was also deposited into the gels carrying carboxyl groups. Although cortical nerve fibers in the surrounding tissue showed a regenerative response, extending onto or into the matrices, this behavior seemed to depend more on the organization of the astrocytic scar imposed by the gel than on the type of gel. We conclude that matrices carrying negatively charged groups influence favorably the astrocytosis and the deposition of connective tissue, and that this approach represents a new avenue in attempting to modulate the brain scar formation.

L5 ANSWER 55 OF 69 MEDLINE
ACCESSION NUMBER: 91076478 MEDLINE
DOCUMENT NUMBER: 91076478 PubMed ID: 2175157
TITLE: Artificial nerve graft using **collagen** as an extracellular matrix for nerve repair compared with sutured autograft in a rat model.
AUTHOR: Rosen J M; Padilla J A; Nguyen K D; Padilla M A; Sabelman E E; Pham H N
CORPORATE SOURCE: Division of Plastic and Reconstructive Surgery, Stanford University School of Medicine, CA 94305.
SOURCE: ANNALS OF PLASTIC SURGERY, (1990 Nov) 25 (5) 375-87.
Journal code: 5VB; 7805336. ISSN: 0148-7043.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199101
ENTRY DATE: Entered STN: 19910308
Last Updated on STN: 19980206
Entered Medline: 19910124
AB A study was conducted to compare the regeneration of rat peroneal nerves across 0.5-cm gaps repaired with artificial nerve grafts versus sutured autografts. The artificial nerve graft model is composed of a synthetic biodegradable passive conduit made of polyglycolic acid filled with a **collagen** extracellular matrix (predominantly Type I **collagen**, derived from calf skin, and with the telopeptide ends left intact). Axonal regeneration was studied in 22 long-term animals (11 or 12 months). The nerves were studied by qualitative and quantitative histological and electrophysiological methods, and by functional analysis in 9 of the animals. The axonal regeneration of the artificial nerve graft is equal to sutured autografts as measured by axonal counts, and by physiological and functional methods, although the sutured autografts demonstrated statistically superior axonal diameters.

L5 ANSWER 56 OF 69 MEDLINE
ACCESSION NUMBER: 91015728 MEDLINE
DOCUMENT NUMBER: 91015728 PubMed ID: 2215922
TITLE: Transected spinal cords grafted with in situ self-assembled **collagen** matrices.
AUTHOR: Marchand R; Woerly S
CORPORATE SOURCE: Centre de recherche en Neurobiologie, Hopital de l'Enfant-Jesus, Quebec, Canada.
SOURCE: NEUROSCIENCE, (1990) 36 (1) 45-60.
Journal code: NZR; 7605074. ISSN: 0306-4522.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199011
ENTRY DATE: Entered STN: 19910117
Last Updated on STN: 19980206
Entered Medline: 19901119

AB The purpose of this work was to evaluate if the implantation into the gap of a transected spinal cord of a biomaterial providing a scaffolding structure for tissue ingrowth would favor the permeation and the growth of regenerating axons across the spinal-bioimplant interface. The interstump gap of rat transected spinal cords was injected with an ice-cold neutral solution of **collagen**, either alone or mixed with glyoxal, a harmless tanning agent. Upon warming to the temperature of the tissue, the fluid implant self-assembled forming a loose fibrillar network which simultaneously re-established a physical continuity to the transected organ. At various post-implantation timepoints, the bioimplants were studied by light microscopy, with the picrosirius-polarization method and with scanning electron microscopy. We observed that the bioimplants evolved following three overlapping phases: first a massive inflammatory response characterized by the invasion of cells of heterogeneous nature, then, a phase where microcysts predominated and during which, there is a major remodeling of the biomatrix by the deposition of newly synthesized **collagen** and of a periodic acid Schiff-positive material. Finally, a regeneration phase occurred where astroglial processes followed by regenerating axons invaded the biomatrix. Three months after implantation, spinal axons had grown from the two spinal stumps and penetrated the bioimplant across at least one lesion interface. However, the glyoxal-tanned **collagen** matrices showed a better biostability and durability than **collagen** alone. We conclude that the histopathological reaction of the mammalian lesioned spinal cord, when adequately directed by a scaffolding structure can be beneficial for the expression of the intrinsic regenerative capacity of the spinal cord tissue.

L5 ANSWER 57 OF 69 MEDLINE
ACCESSION NUMBER: 90275224 MEDLINE
DOCUMENT NUMBER: 90275224 PubMed ID: 2350554
TITLE: Immunogenicity of collagenous **implants**.
AUTHOR: Meade K R; Silver F H
CORPORATE SOURCE: Department of Pathology, UMDNJ-Robert Wood Johnson Medical School, Piscataway 08854.
SOURCE: BIOMATERIALS, (1990 Apr) 11 (3) 176-80.
Journal code: A4P; 8100316. ISSN: 0142-9612.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199007
ENTRY DATE: Entered STN: 19900824
Last Updated on STN: 19980206
Entered Medline: 19900716

AB Collagenous biomaterials have been used in our laboratory for treatment of decubitus ulcers, tendon/ligament repair and **nerve regeneration**. Results of previous studies suggest that **implants** containing bovine type I **collagen** enhance repair and regeneration of connective tissue found in different organs. The purpose of this paper is to evaluate the immunological response to type I **collagen** that is cross-linked using either glutaraldehyde or cyanamide treatment. Humoral and cell mediated responses to type I **collagen** are evaluated in a rabbit model. Results obtained in this study suggest that antibody levels and cell-mediated response to type I **collagen** are highest in animals exposed to uncross-linked implant materials and these responses are increased by booster injections of the antigen. Antibody titres to cross-linked **collagen** are significantly lower than those observed for uncross-linked material. Extensive implant cross-linking does not totally eliminate the humoral response and may lead to a cell-mediated reaction.

L5 ANSWER 58 OF 69 MEDLINE
ACCESSION NUMBER: 90187226 MEDLINE

DOCUMENT NUMBER: 90187226 PubMed ID: 1690226
TITLE: Implantation of cultured sensory neurons and Schwann cells into lesioned neonatal rat spinal cord. II. Implant characteristics and examination of corticospinal tract growth.
AUTHOR: Kuhlengel K R; Bunge M B; Bunge R P; Burton H
CORPORATE SOURCE: Department of Anatomy and Neurobiology, Washington University School of Medicine, St. Louis, Missouri 63110.
CONTRACT NUMBER: NS 09809 (NINDS)
NS 09923 (NINDS)
NS 15070 (NINDS)
SOURCE: JOURNAL OF COMPARATIVE NEUROLOGY, (1990 Mar 1) 293 (1) 74-91.
Journal code: HUV; 0406041. ISSN: 0021-9967.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199004
ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 19960129
Entered Medline: 19900416

AB The purpose of this study was to test the effectiveness of **implants** derived from peripheral neural tissue to serve as bridges following interruption of the developing corticospinal tract (CST). **Implants** prepared from purified populations of cultured dorsal root ganglion neurons (DRGNs) and Schwann cells (SCs) (Kuhlengel et al., J. Comp. Neurol. 293:63-73, 1990) were placed into thoracolumbar regions of neonatal rat spinal cord from which a 2-mm length of dorsal columns had been removed by suction. These cords were examined by a number of techniques 10 days to 6 months later. The **implants**, recognizable by their DRGN content, filled the vacated dorsal columns and survived the longest periods examined. The most effective method to maintain implant position was dorsal placement of **collagen**-coated Nitex filter. **Implants** were inserted either at the time of lesioning or 5 days later. The implant survival rate was better (72% vs. 50%) and meningeal scarring was less with immediate implantation, but delayed implantation resulted in better implant-cord fusion and the implant better filled the lesion cavity. DRGN/SC **implants** became well vascularized without leptomeningeal cells; this may explain why implant survival was not improved with leptomeningeal cell addition. Particularly well-differentiated **implants** (full extracellular matrix production and myelination) did not fuse as well with cord as did those less well differentiated. The addition of nerve growth factor to the Nitex filter **collagen** coating led to improved survival of DRGNs in **implants**. Electron microscopy showed that astrocytes populated the implant-cord junction region and migrated into **implants**. Typical SCs related to nonmyelinated and myelinated axons were present in **implants**. Close proximity of astrocytes and central myelin to SCs and peripheral myelin demonstrated good implant integration with cord. Clusters of SCs, astrocytes, and axons, all enclosed within a common basal lamina, were observed in **implants**. Immunostaining for GFAP and laminin confirmed our microscopy findings that SCs did not migrate from implant into host but that astrocytes left host tissue to enter **implants**. Neuroanatomical tracing of CST neurons with HRP-WGA showed that labeled fibers were not present in the implant but were fasciculated just beneath in gray matter. These fibers remained clustered in gray matter underneath the ventral dorsal columns caudal to the lesion. In lesioned but not implanted rats, labeled fibers were only diffusely distributed in gray matter. Delayed implantation led to more variation in fasciculation compared with immediate implantation.(ABSTRACT TRUNCATED AT 400 WORDS)

L5 ANSWER 59 OF 69 MEDLINE
ACCESSION NUMBER: 90149401 MEDLINE
DOCUMENT NUMBER: 90149401 PubMed ID: 2620177
TITLE: Addition of nerve growth factor to the interior of a tubular prosthesis increases sensory neuron regeneration in vivo.

AUTHOR: Da-Silva C F; Langone F
CORPORATE SOURCE: Departamento de Anatomia, Universidade de Sao Paulo, Brasil.
SOURCE: BRAZILIAN JOURNAL OF MEDICAL AND BIOLOGICAL RESEARCH, (1989) 22 (6) 691-4.
Journal code: BOF; 8112917. ISSN: 0100-879X.
PUB. COUNTRY: Brazil
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199003
ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 19980206
Entered Medline: 19900326

AB The sciatic nerve of adult mice was transected and the proximal and distal nerve stumps were sutured into a polyethylene tube. The tubes were implanted either empty, or the lumen was filled with pure **collagen** or a mixture of **collagen**/nerve growth factor (NGF). Six weeks later, cells in the L3-L5 dorsal root ganglia (DRG) were retrogradely filled with horseradish peroxidase (HRP). The data demonstrate that the addition of NGF to the interior of the tubular prosthesis can significantly increase the regeneration rate of sensory neurons.

L5 ANSWER 60 OF 69 MEDLINE
ACCESSION NUMBER: 90014115 MEDLINE
DOCUMENT NUMBER: 90014115 PubMed ID: 2796717
TITLE: Reliability of sciatic function index in assessing **nerve regeneration** across a 1 cm gap.
AUTHOR: Shenaq J M; Shenaq S M; Spira M
CORPORATE SOURCE: Division of Plastic Surgery, Baylor College of Medicine, Houston, Texas 77030.
CONTRACT NUMBER: RR-00350 (NCRR)
SOURCE: MICROSURGERY, (1989) 10 (3) 214-9.
Journal code: MIS; 8309230. ISSN: 0738-1085.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198911
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 19980206
Entered Medline: 19891109

AB To evaluate the validity of sciatic function index as a reliable functional parameter in assessing regeneration of rat sciatic nerve through a 1 cm gap, we undertook the following investigation. Sixty-three adult male Sprague-Dawley rats were assigned to four groups for repair of a 1 cm gap created in the right rat sciatic nerve; 19 rats were repaired with amniotic **collagen** conduits, 20 with nerve autograft, and 17 with silicone tubes. In seven rats, the gap was not repaired and served as a control. Functional recovery was assessed by de-Medinaceli SFI and by clinical observations, compared with quantitative and qualitative histological results at 4, 10, and 17 weeks postoperatively. The SFI results did not correlate with the histological findings and clinical observations over the observation period in all groups.

L5 ANSWER 61 OF 69 MEDLINE
ACCESSION NUMBER: 89157194 MEDLINE
DOCUMENT NUMBER: 89157194 PubMed ID: 2921658
TITLE: Effect of different surgical repair modalities on regeneration of the rabbit mandibular nerve.
AUTHOR: Eppley B L; Doucet M J; Winkelmann T; Delfino J J
CORPORATE SOURCE: Division of Oral-Maxillofacial Surgery, St John's Mercy Medical Center, St Louis, MO 63141.
SOURCE: JOURNAL OF ORAL AND MAXILLOFACIAL SURGERY, (1989 Mar) 47 (3) 257-76.
Journal code: JIC; 8206428. ISSN: 0278-2391.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Dental Journals; Priority Journals
ENTRY MONTH: 198904
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19980206
Entered Medline: 19890407

AB A study was designed to evaluate the ability of the rabbit mandibular nerve to regenerate when exposed to crush and resection injuries, as well as to determine how differently sized resection injuries healed when repaired with either autogenous grafts or laminin-lined **collagen** tubulization. The nerve demonstrated a regenerative capacity over a 1-cm defect, with morphology and function that approximated normals, but could not span a 2-cm gap defect unaided. Crush injuries produced findings that were inferior to both those in normal nerves and in those with resections. In 1-cm defects, both grafting and tubular repairs produced similar results, with substantial recovery of neural function after 16 weeks. In 2-cm defects, autogenous grafting was superior to tubulization by both morphologic and functional assessment. Replacement of the lateral cortex of the mandible after nerve repair was shown to be unnecessary. The implications of these findings as they relate to nerve injury and repair in humans is discussed.

L5 ANSWER 62 OF 69 MEDLINE
ACCESSION NUMBER: 89141526 MEDLINE
DOCUMENT NUMBER: 89141526 PubMed ID: 2537422
TITLE: Artificial nerve graft compared to autograft in a rat model.
AUTHOR: Rosen J M; Pham H N; Abraham G; Harold L; Hentz V R
CORPORATE SOURCE: Rehabilitation Engineering Research and Development Center, Veterans Administration Medical Center, Palo Alto, CA 94304.
CONTRACT NUMBER: NS 14165-05 (NINDS)
SOURCE: JOURNAL OF REHABILITATION RESEARCH AND DEVELOPMENT, (1989 Winter) 26 (1) 1-14.
Journal code: JRD; 8410047. ISSN: 0748-7711.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198903
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19980206
Entered Medline: 19890327

AB A study was made to compare the regeneration of rat peroneal nerve across a 0.5 cm gap repaired with a sutured autograft (SAG) versus an artificial nerve graft (ANG). The ANG model is composed of a synthetic biodegradable passive conduit made of polyglycolic acid (PGA) and a synthetic growth medium composed of hypoallergenic **collagen**. Axonal regeneration in short-term animals (1 and 4 months) was evaluated by qualitative histology only, while in long-term animals (17 to 21 months) quantitative histology and electro-physiology were used in addition to qualitative histology. This study reveals that axons do regenerate through this ANG model, but electrophysiological analyses show that the axonal regeneration is statistically inferior to that in the SAG. There was no significant statistical difference in the quantitative histological data.

L5 ANSWER 63 OF 69 MEDLINE
ACCESSION NUMBER: 89099434 MEDLINE
DOCUMENT NUMBER: 89099434 PubMed ID: 2911622
TITLE: Exogenous laminin induces regenerative changes in traumatized sciatic and optic nerve.
AUTHOR: Politis M J
CORPORATE SOURCE: Department of Orthopedic Surgery, Shaughnessy Research Centre, Vancouver, British Columbia, Canada.
SOURCE: PLASTIC AND RECONSTRUCTIVE SURGERY, (1989 Feb) 83 (2) 228-35.
Journal code: P9S; 1306050. ISSN: 0032-1052.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198902
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19890223

AB Laminin is an extracellular matrix component which can promote neuritic elongation in vitro and has been implicated in the promotion of **nerve regeneration** in vivo. The present study was undertaken to determine if implantation of Elvax pellets containing exogenous laminin distal to site of lesion could promote regenerative responses in vivo in the adult rat peripheral (sciatic) and central (optic) nerve. In peripheral nerve preparations, Elvax pellets containing laminin or **collagen** were assessed for their ability to "lure" transected axons into 5-mm-long silicone tubes. In optic nerve studies, laminin pellets were inserted distal to site of nerve crush, and the extent of axonal elongation 2.5 mm to the injury site was assessed. Laminin-containing pellets appeared to support appreciable axonal elongation in both systems. This effect was dose-dependent and not exerted by **collagen** pellets, substrate-free pellets, or pellets containing irradiated laminin. **Collagen** IV had some beneficial effect in peripheral, but not central, nerve preparations.

L5 ANSWER 64 OF 69 MEDLINE
ACCESSION NUMBER: 89082916 MEDLINE
DOCUMENT NUMBER: 89082916 PubMed ID: 2905029
TITLE: Increased blood flow enhances axon regeneration after spinal transection.
AUTHOR: de la Torre J C; Goldsmith H S
CORPORATE SOURCE: University of Ottawa Health Sciences, Ont., Canada.
SOURCE: NEUROSCIENCE LETTERS, (1988 Dec 5) 94 (3) 269-73.
Journal code: N7N; 7600130. ISSN: 0304-3940.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198902
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19890206

AB It is not known whether increasing the amount of blood flow to axotomized fibers in mammalian CNS can result in more robust sprouting. To find out, an intact pedicled omentum was surgically transposed to cover a **collagen** matrix gel used to bridge the transected cat spinal cord stumps. Control animals were similarly treated but did not receive the pedicled omentum. Twelve weeks after cord transection, animals receiving the pedicled omentum showed a 66% spinal cord blood flow increase over animals that did not. Moreover, treatment with the pedicled omentum increased the density of regenerating adrenergic axons 10-fold over the control group. These findings indicate that boosting flow with an omental graft to the **collagen** bridge site results in robust axonal outgrowth of spinal transected nerve fibers.

L5 ANSWER 65 OF 69 MEDLINE
ACCESSION NUMBER: 88270052 MEDLINE
DOCUMENT NUMBER: 88270052 PubMed ID: 3390701
TITLE: Entubulation repair with protein additives increases the maximum nerve gap distance successfully bridged with tubular prostheses.
AUTHOR: Madison R D; Da Silva C F; Dikkes P
CORPORATE SOURCE: Department of Neuroscience, Children's Hospital, Boston, MA 02115.
CONTRACT NUMBER: NS22404 (NINDS)
SOURCE: BRAIN RESEARCH, (1988 May 3) 447 (2) 325-34.
Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 198808
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19980206
Entered Medline: 19880812

AB The major objective of the experiments reported in this paper was to test the hypothesis that the maximum distance that peripheral nervous system (PNS) axons can regenerate through a tubular prosthesis may be increased by specific modifications to the internal environment of the prosthesis. The sciatic nerve of adult male rats was transected and proximal and distal nerve stumps were sutured into a silicone tube 20-25 mm in length. The silicone tubes were implanted empty, or the lumen was filled with **collagen** or a laminin-containing gel. Following 4-16 weeks survival time animals were sacrificed and the contents of the silicone tubes were processed for histological identification of myelinated and unmyelinated axons. All of the tubes with additives, but one of the initially empty tubes, displayed a regenerated nerve cable within the tube. Retrograde labeling studies were carried out to prove that some of the axons present in the regenerated nerve cables arose from primary motor and sensory neurons. These results show that specific modifications to the microenvironment of regenerating PNS axons can affect the success or failure of tubular prostheses for nerve repair.

L5 ANSWER 66 OF 69 MEDLINE
ACCESSION NUMBER: 88051872 MEDLINE
DOCUMENT NUMBER: 88051872 PubMed ID: 3676722
TITLE: Morphological response of injured adult rabbit optic nerve to **implants** containing media conditioned by growing optic nerves.
AUTHOR: Lavie V; Harel A; Doron A; Solomon A; Lobel D; Belkin M; Ben-Basat S; Sharma S; Schwartz M
CORPORATE SOURCE: Department of Neurobiology, Weizmann Institute of Science, Rehovot, Israel.
SOURCE: BRAIN RESEARCH, (1987 Sep 1) 419 (1-2) 166-72.
Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198801
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19880111

AB Adult rabbit retina can express regeneration-associated characteristics after optic nerve injury, provided it is supplied with appropriate diffusible substances originating from media conditioned by regenerating fish optic nerves or by optic nerves of a newborn rabbit [Hadani et al., Proc. Natl. Acad. Sci. U.S.A., 81 (1984) 7965; Schwartz et al., Science, 228 (1985) 600]. This was shown by applying the active substances to the injured axons in the form of 'wrap-around' **implants**, consisting of **collagen**-coated silicone tubes which had been soaked in the conditioned media (CM). The regeneration-associated response was manifested biochemically and by sprouting of nerve fibers in culture. The present work provides morphological evidence that the implantation prolongs survival of ganglion cells and optic nerve fibers and induces new growth. Light microscopic analysis (using horseradish peroxidase (HRP) for labeling the fibers) revealed, 1 week following optic nerve injury, labeled fibers and ganglion cells in both the implanted and control (injured only or injured and implanted with **collagen**-coated silicone tubes free of CM) nerves. However, from the second week after the injury, distinct differences in the appearance of viable ganglion cells and labeled fibers, were seen between experimental and control preparations. In sections taken through the optic nerve, at the region distal to the site of injury, HRP-labeled fibers were seen in the experimental nerves 1 week, 2 weeks and to a significantly lesser extent 1 month after injury.(ABSTRACT TRUNCATED AT 250 WORDS)

L5 ANSWER 67 OF 69 MEDLINE
ACCESSION NUMBER: 87049363 MEDLINE
DOCUMENT NUMBER: 87049363 PubMed ID: 3778752

TITLE: Regeneration of transected sciatic nerves through semi-permeable nerve guidance channels. Effects of extracellular matrix protein additives.
AUTHOR: Aebischer P; Valentini R F; Winn S R; Kunz S; Sasken H; Galletti P M
SOURCE: ASAIO TRANSACTIONS, (1986 Jul-Sep) 32 (1) 474-7.
Journal code: ASA; 8611947. ISSN: 0889-7190.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198701
ENTRY DATE: Entered STN: 19900302
Last Updated on STN: 19980206
Entered Medline: 19870112

L5 ANSWER 68 OF 69 MEDLINE
ACCESSION NUMBER: 85051711 MEDLINE
DOCUMENT NUMBER: 85051711 PubMed ID: 6209159
TITLE: Nontoxic nerve guide tubes support neovascular growth in transected rat optic nerve.
AUTHOR: Madison R; Sidman R L; Nyilas E; Chiu T H; Greatorex D
CONTRACT NUMBER: EY04730 (NEI)
NS14768 (NINDS)
SOURCE: EXPERIMENTAL NEUROLOGY, (1984 Dec) 86 (3) 448-61.
Journal code: EQF; 0370712. ISSN: 0014-4886.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198501
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19980206
Entered Medline: 19850123
AB Nontoxic, bioresorbable "nerve guide" tubes were used to bridge the transected optic nerves of adult rats. Nerve guides were fabricated as polymers of synthetic poly D,L-lactates with 2% triethyl citrate added as a plasticizer. The local environment was manipulated further by the addition of the proteins **collagen**, fibrinogen, and anti-Thy-1 antibody to the nerve guide lumens at the time of operation. Neovascular growth through the nerve guide lumens was quantified with the aid of a computer-controlled microscope. Neovascular growth was greater in the nerve guides to which proteins had been added, compared with initially empty nerve guides. These experiments demonstrated the effectiveness of these nerve guide tubes in supporting and directing neovascular growth in the mammalian central nervous system, and suggested that specific alterations of the local environment within the nerve guide lumen can affect the extent of neovascular growth.

L5 ANSWER 69 OF 69 MEDLINE
ACCESSION NUMBER: 75089912 MEDLINE
DOCUMENT NUMBER: 75089912 PubMed ID: 4447483
TITLE: Rehabilitation of vocal cord paralysis. Studies using the vagus recurrent bypass anastomosis, type ramus posterior shunt.
AUTHOR: Miehlike A
SOURCE: ARCHIVES OF OTOLARYNGOLOGY, (1974 Dec) 100 (6) 431-41.
Journal code: 86O; 0376526. ISSN: 0003-9977.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197504
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19750417

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NEWS 24	Nov 30	Files VETU and VETB to have open access
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```
DULICATE IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> DUPLICATE REMOVE
ENTER L# LIST OR (END):L5
DUPLICATE PREFERENCE IS 'BIOSIS, CAPLUS, MEDLINE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):N
PROCESSING COMPLETED FOR L5
L6            61 DUPLICATE REMOVE L5 (8 DUPLICATES REMOVED)

=> D HIS

     (FILE 'HOME' ENTERED AT 14:50:53 ON 10 DEC 2001)

     FILE 'BIOSIS, CAPLUS, MEDLINE' ENTERED AT 14:51:26 ON 10 DEC 2001
L1         92198 S IMPLANTS
L2        233782 S COLLAGEN
L3         15971 S NERVE (W) REGENERATION
L4          3929 S L1 AND L2
L5            69 S L3 AND L4
L6            61 DUPLICATE REMOVE L5 (8 DUPLICATES REMOVED)
```

FULL ESTIMATED COST 0.15 0.15

FILE 'BIOSIS' ENTERED AT 15:17:53 ON 10 DEC 2001
COPYRIGHT (C) 2001 BIOSIS(R)

FILE 'CAPLUS' ENTERED AT 15:17:53 ON 10 DEC 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 15:17:53 ON 10 DEC 2001

=> S IMPLANTS
L1 92198 IMPLANTS

=> S COLLAGEN
L2 233782 COLLAGEN

=> S NERVE (W) REGENERATION
L3 15971 NERVE (W) REGENERATION

=> S L1 AND L2
L4 3929 L1 AND L2

=> S L4 AND L3
L5 69 L4 AND L3

=> S TYPE (W) I (W) COLLAGEN
L6 18290 TYPE (W) I (W) COLLAGEN

=> S TYPE (W) III (W) COLLAGEN
L7 5051 TYPE (W) III (W) COLLAGEN

=> S TYPE (W) IV (W) COLLAGEN
L8 11105 TYPE (W) IV (W) COLLAGEN

=> REMOVE DUPLICATES L5
DUPLICATES IS NOT VALID HERE
The DELETE command is used to remove various items stored by the system.

To delete a saved query, saved answer set, saved L-number list, SDI request, batch request, mailing list, or user-defined cluster, format, or search field, enter the name. The name may include ? for left, right, or simultaneous left and right truncation.

Examples:

```
  DELETE BIO?/Q           - delete query names starting with BIO
  DELETE ?DRUG/A          - delete answer set names ending with DRUG
  DELETE ?ELEC?/L         - delete L-number lists containing ELEC
  DELETE ANTICOAG/S       - delete SDI request
  DELETE ENZYME/B         - delete batch request
  DELETE .MYCLUSTER       - delete user-defined cluster
  DELETE .MYFORMAT        - delete user-defined display format
  DELETE .MYFIELD         - delete user-defined search field
  DELETE NAMELIST MYLIST - delete mailing list
```

To delete an ordered document or an offline print, enter its number.

Examples:

```
  DELETE P123001C         - delete print request
  DELETE D134002C         - delete document order request
```

To delete an individual L-number or range of L-numbers, enter the L-number or L-number range. You may also enter DELETE LAST followed by a number, n, to delete the last n L-numbers. RENUMBER or

NORENUMBER may also be explicitly specified to override the value of
SET RENUMBER.

Examples:

```
  DELETE L21             - delete a single L-number
  DELETE L3-L6           - delete a range of L-numbers
  DELETE LAST 4          - delete the last 4 L-numbers
  DELETE L33-            - delete L33 and any higher L-number
  DELETE -L55            - delete L55 and any lower L-number
  DELETE L2-L6 RENUMBER - delete a range of L-numbers and
                          renumber remaining L-numbers
  DELETE RENUMBER        - renumber L-numbers after deletion of
                          intermediate L-numbers
```

Entire sets of saved items, SDI requests, batch requests, user-defined
items, or E-numbers can be deleted.

Examples:

```
  DELETE SAVED/Q - delete all saved queries
  DELETE SAVED/A - delete all saved answer sets
  DELETE SAVED/L - delete all saved L-number lists
  DELETE SAVED   - delete all saved queries, answer sets,
                   and L-number lists
  DELETE SAVED/S - delete all SDI requests
  DELETE SAVED/B - delete all batch requests
  DELETE CLUSTER - delete all user-defined clusters
  DELETE FORMAT  - delete all user-defined display formats
  DELETE FIELD   - delete all user-defined search fields
  DELETE SELECT  - delete all E-numbers
  DELETE HISTORY - delete all L-numbers and restart the
                   session at L1
```

To delete an entire multifile SDI request, enter DELETE and
the name of the request. To delete a component from the
multifile SDI, enter DELETE and the name of the component.

```
=> D HIS

     (FILE 'HOME' ENTERED AT 15:17:07 ON 10 DEC 2001)

     FILE 'BIOSIS, CAPLUS, MEDLINE' ENTERED AT 15:17:53 ON 10 DEC 2001
L1         92198 S IMPLANTS
L2        233782 S COLLAGEN
L3         15971 S NERVE (W) REGENERATION
L4          3929 S L1 AND L2
L5            69 S L4 AND L3
L6         18290 S TYPE (W) I (W) COLLAGEN
L7          5051 S TYPE (W) III (W) COLLAGEN
L8         11105 S TYPE (W) IV (W) COLLAGEN

=> S L5 AND L6
L9             8 L5 AND L6

=> S L5 AND L7
L10            0 L5 AND L7

=> S L5 AND L8
L11            0 L5 AND L8

=> D L9 IBIB ABS 1-8

L9   ANSWER 1 OF 8  BIOSIS  COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER:   1996:118186  BIOSIS
DOCUMENT NUMBER:    PREV199698690321
TITLE:              Recent advances in tissue synthesis in vivo by use of
                    collagen- glycosaminoglycan copolymers.
AUTHOR(S):          Ellis, D. L.; Yannas, I. V. (1)
```

implant cell Nerves / Type I

CORPORATE SOURCE: (1) Dep. Mech. Eng., 77 Massachusetts Ave., Mass. Inst. Technol., Cambridge, MA 02139 USA
SOURCE: Biomaterials, (1996) Vol. 17, No. 3, pp. 291-299. ISSN: 0142-9612.
DOCUMENT TYPE: General Review
LANGUAGE: English

AB Biologically active analogues of the extracellular matrix (ECM) are synthesized by grafting glycosaminoglycan (GAG) chains onto **type I collagen**, and by controlling the physicochemical properties of the resulting graft copolymer. **Collagen**-GAG ECM analogues have previously been shown to induce regeneration of the dermis in humans and the guinea pig, and of the rat sciatic nerve. Current studies have emphasized elucidation of the molecular mechanism through which tissue-specific ECM analogues induce regeneration. The contribution of the GAGs to the biological activity of the skin regeneration template was confirmed by studying the contribution of several GAGs to the inhibition of wound contraction in guinea pigs. The interaction between cells and the porous structure of an ECM analogue was studied with emphasis on the deformation of pores which occurs during wound contraction. The synthesis of scar, as well as of partly regenerated tissue which has a morphology between that appropriate for scar and for normal dermis, was quantitatively assayed for the first time using a laser light scattering technique. An ECM analogue which has been shown to be capable of inducing regeneration of functional sciatic nerve in the rat over a gap larger than 10 mm was incorporated in the design of a biodegradable implant for peripheral **nerve regeneration**
.

L9 ANSWER 2 OF 8 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1990:285361 BIOSIS
DOCUMENT NUMBER: BA90:16207
TITLE: IMMUNOGENICITY OF COLLAGENOUS **IMPLANTS**.
AUTHOR(S): MEADE K R; SILVER F H
CORPORATE SOURCE: BIOMATERIALS CENT., DEP. PATHOL., UMDNJ-ROBERT WOOD JOHNSON MED. SCH., 675 HOES LANES, PISCATAWAY, N.J. 08854, USA.
SOURCE: BIOMATERIALS, (1990) 11 (3), 176-180. CODEN: BIMADU. ISSN: 0142-9612.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Collagenous biomaterials have been used in our laboratory for treatment of decubitus ulcers, tendon/ligament repair and **nerve regeneration**. Results of previous studies suggest that **implants** containing bovine **type I collagen** enhance repair and regeneration of connective tissue found in different organs. The purpose of this paper is to evaluate the immunological response to **type I collagen** that is cross-linked using either glutaraldehyde or cyanamide treatment. Humoral and cell mediated responses to **type I collagen** are evaluated in a rabbit model. Results obtained in this study suggest that antibody levels and cell-mediated response to **type I collagen** are highest in animals exposed to uncross-linked implant material and these responses are increased by booster injections of the antigen. Antibody titres to cross-linked **collagen** are significantly lower than those observed for uncross-linked material. Extensive implant cross-linking does not totally eliminate the humoral response and may lead to a cell-mediated reaction.

L9 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:452508 CAPLUS
DOCUMENT NUMBER: 132:98057
TITLE: Magnetically aligned **collagen** gel filling a **collagen** nerve guide improves peripheral **nerve regeneration**
AUTHOR(S): Ceballos, Dolores; Navarro, Xavier; Dubey, Naren; Wendelschafer-Crabb, Gwen; Kennedy, William R.; Tranquillo, Robert T.
CORPORATE SOURCE: Department of Neurology, University of Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Exp. Neurol. (1999), 158(2), 290-300

longitudinal
Type I

CODEN: EXNEAC; ISSN: 0014-4886
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bioresorbable **collagen** nerve guides filled with either magnetically aligned **type I collagen** gel or control **collagen** gel were implanted into 4- or 6-mm surgical gaps created in the sciatic nerve of mice and explanted 30 and 60 days postoperation (dpo) for histol. and immunohistochem. evaluation. The hypothesis was that contact guidance of regenerating axons and/or invading nonneuronal cells to the longitudinally aligned **collagen** fibrils would improve **nerve regeneration**. The criterion for regeneration was observation of regenerating myelinated fibers distal to the nerve guide. Consistent with previous studies showing poor regeneration in 6-mm gaps at 60 dpo with entubulation repair, only one of six mice exhibited regeneration with control **collagen** gel. In contrast, four of four mice exhibited regeneration with magnetically aligned **collagen** gel, including the appearance of nerve fascicle formation. The nos. of myelinated fibers were less than the uninjured nerve in all groups, however, which may have been due to rapid resorption of the nerve guides. An attempt to increase the stability of the **collagen** gel; and thereby the directional information presented by the aligned **collagen** fibrils, by crosslinking the **collagen** with ribose before implantation proved detrimental for regeneration. (c) 1999 Academic Press.

aligned collagen
ie longitudinal orientation

REFERENCE COUNT: 48
REFERENCE(S):
(3) Archibald, S; J Neurosci 1995, V15, P4109 CAPLUS
(8) Girton, T; J Biomed Mat Res 1999, V46, P87 CAPLUS
(13) Henry, E; Exp Neurol 1985, V90, P652 CAPLUS
(15) King, G; Endocrinol Metab Clin North Am 1996, V25, P255 CAPLUS
(16) Labrador, R; Exp Neurol 1998, V149, P243 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 8 MEDLINE
ACCESSION NUMBER: 95153321 MEDLINE
DOCUMENT NUMBER: 95153321 PubMed ID: 7850464
TITLE: Sciatic **nerve regeneration** navigated by laminin-fibronectin double coated biodegradable **collagen** grafts in rats.
AUTHOR: Tong X J; Hirai K; Shimada H; Mizutani Y; Izumi T; Toda N; Yu P
CORPORATE SOURCE: Department of Anatomy, Kanazawa Medical University, Ishikawa, Japan.
SOURCE: BRAIN RESEARCH, (1994 Nov 7) 663 (1) 155-62.
Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950322
Last Updated on STN: 19950322
Entered Medline: 19950314

longitudinal laminin type I

AB Biodegradable **type I collagen** tube grafts filled longitudinally with laminin and fibronectin double coated **collagen** fiber bundles (L-F grafts) were implanted to promote sciatic **nerve regeneration** in rats. Grafts filled with uncoated **collagen** fibers were used as control. A 1 cm defect on the right sciatic nerve was filled with a graft in the manner of bridging. Thirty days after implantation, several newly developed nerve fasciculi were found at the middle portion of the L-F grafts in contrast to no developed nerves in the controls. After 60 days, the middle and distal portions of both grafts included well-developed nerve tissues with prominent myelinated and unmyelinated nerve fibers surrounded by perineural cells, but the control distal portion showed fewer nerve fibers. All artificial **collagen** elements were completely degraded and absorbed at 30 days, and new nerve tissues surrounded by an epineurium successfully connected the proximal stump to the distal stump

of the initially separated nerve. Descending and ascending action potentials were evoked in all grafts at 60 days. These results indicated that laminin and fibronectin may promote the growth of axons in biodegradable **collagen** grafts, which guided **nerve regeneration** well and allowed the formation of epineurium.

L9 ANSWER 5 OF 8 MEDLINE
ACCESSION NUMBER: 94133208 MEDLINE
DOCUMENT NUMBER: 94133208 PubMed ID: 8301632
TITLE: Sciatic **nerve regeneration** across gaps within **collagen** chambers: the influence of epidermal growth factor.
AUTHOR: Dubuisson A S; Beuermann R W; Kline D G
CORPORATE SOURCE: Department of Neurosurgery, Louisiana State University Medical Center, New Orleans.
SOURCE: JOURNAL OF RECONSTRUCTIVE MICROSURGERY, (1993 Sep) 9 (5) 341-6; discussion 346-7.
PUB. COUNTRY: Journal code: JVX; 8502670. ISSN: 0743-684X.
LANGUAGE: United States
FILE SEGMENT: Journal; Article; (JOURNAL ARTICLE)
ENTRY MONTH: English
ENTRY DATE: Priority Journals
199403
Entered STN: 19940318
Last Updated on STN: 20000303
Entered Medline: 19940307

AB The effects of Epidermal Growth Factor (EGF) on axonal regeneration of a sectioned sciatic nerve within **collagen** tubes were investigated in 15 rats. Following baseline electrophysiologic assessment, bilateral 7-mm nerve gaps were created and repaired by interposition of **collagen** tubes, into which EGF (left side) or **type I collagen** (right side) was instilled. After 4 or 8 weeks, axonal regeneration, measured by electrophysiologic and histologic means, was identical for the EGF and control legs. The conclusion is that EGF does not influence **nerve regeneration** within a **collagen** chamber.

L9 ANSWER 6 OF 8 MEDLINE
ACCESSION NUMBER: 92251670 MEDLINE
DOCUMENT NUMBER: 92251670 PubMed ID: 1315866
TITLE: Artificial nerve graft using glycolide trimethylene carbonate as a nerve conduit filled with **collagen** compared to sutured autograft in a rat model.
AUTHOR: Rosen J M; Padilla J A; Nguyen K D; Siedman J; Pham H N
CORPORATE SOURCE: Division of Plastic and Reconstructive Surgery, Stanford University Medical Center, Palo Alto, CA 94305.
SOURCE: JOURNAL OF REHABILITATION RESEARCH AND DEVELOPMENT, (1992 Spring) 29 (2) 1-12.
PUB. COUNTRY: Journal code: JRD; 8410047. ISSN: 0748-7711.
LANGUAGE: United States
FILE SEGMENT: Journal; Article; (JOURNAL ARTICLE)
ENTRY MONTH: English
ENTRY DATE: Priority Journals
199206
Entered STN: 19920619
Last Updated on STN: 19980206
Entered Medline: 19920611

AB A study was conducted to compare the regeneration of rat peroneal nerves across 0.5 cm gaps repaired with artificial nerve grafts (ANG) versus sutured autografts (SAG). The ANG model is composed of a synthetic biodegradable passive conduit made of glycolide trimethylene carbonate (GTMC) filled with a **collagen** matrix (predominantly **Type I collagen**, derived from calf skin, and with the telopeptide ends left intact). Axonal regeneration was studied in 11 long-term animals (two at 6 months and nine at 9 months). The nerves were studied by qualitative and quantitative histological, electrophysiological, and functional assays. Axonal regeneration with the ANG was equal to SAGs as measured by axonal diameters, physiological, and functional methods, although the SAG demonstrated statistically higher

Type I

axonal counts.

L9 ANSWER 7 OF 8 MEDLINE
ACCESSION NUMBER: 91076478 MEDLINE
DOCUMENT NUMBER: 91076478 PubMed ID: 2175157
TITLE: Artificial nerve graft using **collagen** as an extracellular matrix for nerve repair compared with sutured autograft in a rat model.
AUTHOR: Rosen J M; Padilla J A; Nguyen K D; Padilla M A; Sabelman E E; Pham H N
CORPORATE SOURCE: Division of Plastic and Reconstructive Surgery, Stanford University School of Medicine, CA 94305.
SOURCE: ANNALS OF PLASTIC SURGERY, (1990 Nov) 25 (5) 375-87. Journal code: 5VB; 7805336. ISSN: 0148-7043.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199101
ENTRY DATE: Entered STN: 19910308
Last Updated on STN: 19980206
Entered Medline: 19910124

AB A study was conducted to compare the regeneration of rat peroneal nerves across 0.5-cm gaps repaired with artificial nerve grafts versus sutured autografts. The artificial nerve graft model is composed of a synthetic biodegradable passive conduit made of polyglycolic acid filled with a **collagen** extracellular matrix (predominantly **Type I collagen**, derived from calf skin, and with the telopeptide ends left intact). Axonal regeneration was studied in 22 long-term animals (11 or 12 months). The nerves were studied by qualitative and quantitative histological and electrophysiological methods, and by functional analysis in 9 of the animals. The axonal regeneration of the artificial nerve graft is equal to sutured autografts as measured by axonal counts, and by physiological and functional methods, although the sutured autografts demonstrated statistically superior axonal diameters.

L9 ANSWER 8 OF 8 MEDLINE
ACCESSION NUMBER: 90275224 MEDLINE
DOCUMENT NUMBER: 90275224 PubMed ID: 2350554
TITLE: Immunogenicity of collagenous **implants**.
AUTHOR: Meade K R; Silver F H
CORPORATE SOURCE: Department of Pathology, UMDNJ-Robert Wood Johnson Medical School, Piscataway 08854.
SOURCE: BIOMATERIALS, (1990 Apr) 11 (3) 176-80. Journal code: A4P; 8100316. ISSN: 0142-9612.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199007
ENTRY DATE: Entered STN: 19900824
Last Updated on STN: 19980206
Entered Medline: 19900716

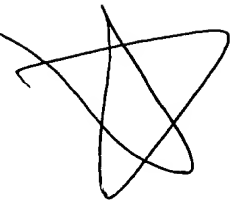
AB Collagenous biomaterials have been used in our laboratory for treatment of decubitus ulcers, tendon/ligament repair and **nerve regeneration**. Results of previous studies suggest that **implants** containing bovine **type I collagen** enhance repair and regeneration of connective tissue found in different organs. The purpose of this paper is to evaluate the immunological response to **type I collagen** that is cross-linked using either glutaraldehyde or cyanamide treatment. Humoral and cell mediated responses to **type I collagen** are evaluated in a rabbit model. Results obtained in this study suggest that antibody levels and cell-mediated response to **type I collagen** are highest in animals exposed to uncross-linked implant materials and these responses are increased by booster injections of the antigen. Antibody titres to cross-linked **collagen** are significantly lower than those observed for

uncross-linked material. Extensive implant cross-linking does not totally eliminate the humoral response and may lead to a cell-mediated reaction.

```
=> D HIS

     (FILE 'HOME' ENTERED AT 15:17:07 ON 10 DEC 2001)

     FILE 'BIOSIS, CAPLUS, MEDLINE' ENTERED AT 15:17:53 ON 10 DEC 2001
L1         92198 S IMPLANTS
L2        233782 S COLLAGEN
L3         15971 S NERVE (W) REGENERATION
L4          3929 S L1 AND L2
L5            69 S L4 AND L3
L6         18290 S TYPE (W) I (W) COLLAGEN
L7          5051 S TYPE (W) III (W) COLLAGEN
L8         11105 S TYPE (W) IV (W) COLLAGEN
L9             8 S L5 AND L6
L10            0 S L5 AND L7
L11            0 S L5 AND L8

=> D L7 AND L6
L6 IS NOT VALID HERE
For an explanation, enter "HELP DISPLAY".

=> S L7 AND L6
L12        2183 L7 AND L6

=> S  L8 ADN L6
MISSING OPERATOR L8 ADN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> S L8 AND L6
L13        1542 L8 AND L6

=> L3 AND L12
L3 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> S L3 AND L12
L14           3 L3 AND L12

=> S L3 AND L13
L15           3 L3 AND L13

=> D HIS

     (FILE 'HOME' ENTERED AT 15:17:07 ON 10 DEC 2001)

     FILE 'BIOSIS, CAPLUS, MEDLINE' ENTERED AT 15:17:53 ON 10 DEC 2001
L1         92198 S IMPLANTS
L2        233782 S COLLAGEN
L3         15971 S NERVE (W) REGENERATION
L4          3929 S L1 AND L2
L5            69 S L4 AND L3
L6         18290 S TYPE (W) I (W) COLLAGEN
L7          5051 S TYPE (W) III (W) COLLAGEN
L8         11105 S TYPE (W) IV (W) COLLAGEN
L9             8 S L5 AND L6
L10            0 S L5 AND L7
L11            0 S L5 AND L8
L12         2183 S L7 AND L6
L13         1542 S L8 AND L6
L14            3 S L3 AND L12
L15            3 S L3 AND L13
```

=> D L14 IBIB ABS

L14 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:634264 CAPLUS
DOCUMENT NUMBER: 130:36800
TITLE: Expression of type I and III collagen and laminin .beta.1 after rat sciatic nerve crush injury
AUTHOR(S): Siironen, Jari; Vuorio, Eero; Sandberg, Minna; Roytta, Matias
CORPORATE SOURCE: Department of Pathology, University of Turku, Turku, 20520, Finland
SOURCE: J. Peripher. Nerv. Syst. (1996), 1(3), 209-221
CODEN: JPNSFO; ISSN: 1085-9489
PUBLISHER: Woodland Publications
DOCUMENT TYPE: Journal
LANGUAGE: English



Type I and III

laminin

AB Extracellular matrix changes are thought to be essential to the regeneration of peripheral nerves. The prodn. of this matrix is believed to be regulated by interactions between axons and their supporting cells. In this study matrix prodn. and cell proliferation were studied during rat sciatic **nerve regeneration** after a crush injury, and compared to that after rat sciatic nerve transection. Expression of pro.alpha.1(I) and pro.alpha.1(III) collagen and laminin .beta.1 mRNAs was followed in isolated endoneuria by Northern and in situ hybridization both proximally and distally to the site of either a crush injury or transection of rat sciatic nerve up to 18 wk. Changes in the Schwann cell and fibroblast populations were monitored by morphometric anal. of endoneurial cross-sections immunostained for S-100 protein. The process of axonal regeneration was followed by Bielschowsky's silver staining. A crush injury initially resulted in increased expression of all mRNAs studied in the endoneurial cells. However, with progressing axonal regeneration the amt. of collagen mRNAs returned to control levels, whereas the amt. of laminin .beta.1 mRNA in the distal site of the crush remained elevated throughout the study period. The expression of **type I collagen** mRNA was enhanced after nerve transection injury compared to that after the crush injury. The epineurial fibroblasts actively expressed both type I and III collagen mRNAs after the injury. The proliferation of Schwann cells and the expression of collagen mRNAs are not, at least directly, related to the axonal regeneration. However, the long-lasting and strong expression of laminin .beta.1 mRNA after a nerve crush injury may be related to good axonal regeneration. The expression of **type I collagen** in the epineurium may lead to clin. well-recognized epineurial scarring and thus impede axonal regeneration.

REFERENCE COUNT: 76
REFERENCE(S):
(1) Baichwal, R; Biochem Biophys Res Commun 1989, V164, P883 CAPLUS
(2) Baichwal, R; Proc Natl Acad Sci USA 1988, V85, P1701 CAPLUS
(3) Barlow, D; EMBO J 1984, V3, P2355 CAPLUS
(6) Bignami, A; J Neuropathol Exp Neurol 1984, V43, P94 CAPLUS
(9) Burgeson, R; Matrix Biology 1994, V14, P209 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D HIS

(FILE 'HOME' ENTERED AT 15:17:07 ON 10 DEC 2001)

FILE 'BIOSIS, CAPLUS, MEDLINE' ENTERED AT 15:17:53 ON 10 DEC 2001
L1 92198 S IMPLANTS
L2 233782 S COLLAGEN
L3 15971 S NERVE (W) REGENERATION
L4 3929 S L1 AND L2
L5 69 S L4 AND L3
L6 18290 S TYPE (W) I (W) COLLAGEN
L7 5051 S TYPE (W) III (W) COLLAGEN
L8 11105 S TYPE (W) IV (W) COLLAGEN

L9	8	S	L5 AND L6
L10	0	S	L5 AND L7
L11	0	S	L5 AND L8
L12	2183	S	L7 AND L6
L13	1542	S	L8 AND L6
L14	3	S	L3 AND L12
L15	3	S	L3 AND L13

=> D L14 IBIB ABS 1-3

L14 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:634264 CAPLUS
DOCUMENT NUMBER: 130:36800
TITLE: Expression of type I and III collagen and laminin .beta.1 after rat sciatic nerve crush injury
AUTHOR(S): Siironen, Jari; Vuorio, Eero; Sandberg, Minna; Roytta, Matias
CORPORATE SOURCE: Department of Pathology, University of Turku, Turku, 20520, Finland
SOURCE: J. Peripher. Nerv. Syst. (1996), 1(3), 209-221
CODEN: JPNSFO; ISSN: 1085-9489
PUBLISHER: Woodland Publications
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Extracellular matrix changes are thought to be essential to the regeneration of peripheral nerves. The prodn. of this matrix is believed to be regulated by interactions between axons and their supporting cells. In this study matrix prodn. and cell proliferation were studied during rat sciatic **nerve regeneration** after a crush injury, and compared to that after rat sciatic nerve transection. Expression of pro.alpha.1(I) and pro.alpha.1(III) collagen and laminin .beta.1 mRNAs was followed in isolated endoneuria by Northern and in situ hybridization both proximally and distally to the site of either a crush injury or transection of rat sciatic nerve up to 18 wk. Changes in the Schwann cell and fibroblast populations were monitored by morphometric anal. of endoneurial cross-sections immunostained for S-100 protein. The process of axonal regeneration was followed by Bielschowsky's silver staining. A crush injury initially resulted in increased expression of all mRNAs studied in the endoneurial cells. However, with progressing axonal regeneration the amt. of collagen mRNAs returned to control levels, whereas the amt. of laminin .beta.1 mRNA in the distal site of the crush remained elevated throughout the study period. The expression of **type I collagen** mRNA was enhanced after nerve transection injury compared to that after the crush injury. The epineurial fibroblasts actively expressed both type I and III collagen mRNAs after the injury. The proliferation of Schwann cells and the expression of collagen mRNAs are not, at least directly, related to the axonal regeneration. However, the long-lasting and strong expression of laminin .beta.1 mRNA after a nerve crush injury may be related to good axonal regeneration. The expression of **type I collagen** in the epineurium may lead to clin. well-recognized epineurial scarring and thus impede axonal regeneration.

REFERENCE COUNT: 76
REFERENCE(S):
(1) Baichwal, R; Biochem Biophys Res Commun 1989, V164, P883 CAPLUS
(2) Baichwal, R; Proc Natl Acad Sci USA 1988, V85, P1701 CAPLUS
(3) Barlow, D; EMBO J 1984, V3, P2355 CAPLUS
(6) Bignami, A; J Neuropathol Exp Neurol 1984, V43, P94 CAPLUS
(9) Burgeson, R; Matrix Biology 1994, V14, P209 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:633122 CAPLUS
DOCUMENT NUMBER: 127:317607
TITLE: Schwann cell extracellular matrix protein production is modulated by Mycobacterium leprae and macrophage secretory products

AUTHOR(S): Singh, Neeta; Birdi, Tannaz J.; Chandrashekar, Sushila; Antia, Noshir H.
CORPORATE SOURCE: The Foundation for Medical Research, 84-A, R.G. Thadani Marg, Worli, Bombay, 400 018, India
SOURCE: J. Neurol. Sci. (1997), 151(1), 13-22
CODEN: JNSCAG; ISSN: 0022-510X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Extracellular matrix (ECM) protein deposition is an important feature of leprous nerves, where Schwann cells (SCs) and macrophages are the main hosts for Mycobacterium leprae. Since, SCs are involved in the synthesis of ECM proteins and its prodn. is regulated by macrophage secretory factors, the present study aimed to det. in vitro, the effect of M. leprae infection and macrophage secretory products on secretion of ECM proteins by SCs in two strains of mice, Swiss White (SW) and C57BL/6, that are known to differ in their nerve pathol. and macrophage functions in response to infection. Following six days of M. leprae infection, SCs from SW mice responded with increased secretion of 14C-leucine radiolabeled proteins and a concomitant increase in laminin and collagens type I, III and IV, as detd. by ELISA. In contrast infected C57BL/6 SCs responded with decreased secretion of total proteins and fibronectin. Exposure of SCs to macrophage conditioned medium resulted in decreased ECM protein secretion in both strains of mice. This decrease was a function of protein breakdown by macrophage derived proteases and also active regulation by macrophage secreted cytokines. A similar effect of M. leprae and macrophage secretory products on SC metab. in leprous nerves would have major ramifications on damage and repair activities. In addn. ECM proteins would also influence the compn. of the infiltrating cell population in lepromatous and tuberculoid nerves.

L14 ANSWER 3 OF 3 MEDLINE
ACCESSION NUMBER: 95274358 MEDLINE
DOCUMENT NUMBER: 95274358 PubMed ID: 7538721
TITLE: Axonal regeneration into chronically denervated distal stump. 2. Active expression of **type I collagen** mRNA in epineurium.
AUTHOR: Siironen J; Vuorinen V; Taskinen H S; Roytta M
CORPORATE SOURCE: Department of Pathology, University of Turku, Finland.
SOURCE: ACTA NEUROPATHOLOGICA, (1995) 89 (3) 219-26.
Journal code: 1CE; 0412041. ISSN: 0001-6322.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950629
Last Updated on STN: 19960129
Entered Medline: 19950620

AB During the first 2 weeks after an injury to peripheral nerve, endoneurial cells proliferate and express integrin beta 1 and mRNA for collagen types I and III. Clinical results for surgical repair within this time are clearly better than those obtained after delayed (months after original injury) surgery. The question of whether this is due to changes in the proliferative capacity of endoneurial cells or to changes in expression of mRNA for collagen types I and III or integrin beta 1 was studied using rats. The left common peroneal nerve was transected and allowed to degenerate for 3 and 6 months. After these times, the tibial nerve of the same animals were transected, and the fresh proximal stump of the transected tibial nerve was sutured into the chronically denervated distal stump of the common peroneal nerve. At 3 and 6 weeks after the reoperation, samples were collected from the distal stump for morphometry, immunohistochemistry and in situ hybridization. Proliferating cells and Schwann cells were identified by immunohistochemistry. These cells increased markedly in number during the axonal reinnervation. In situ hybridization revealed that in the epineurium and perineurium, which were fibrotic, especially type I but also **type III collagen** mRNA were highly expressed. The amount of **type I collagen** mRNA in the endoneurium seemed to increase

Type I & III Retained for

with progressing axonal reinnervation. Immunostaining for integrin beta 1 was negative in these distal stumps. In the present study the proliferation of endoneurial cells and expression of **type I collagen** mRNA in the endoneurium were similar to those found after immediate regeneration of transected peripheral nerve. (ABSTRACT TRUNCATED AT 250 WORDS)

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FILE 'BIOSIS, CAPLUS, MEDLINE' ENTERED AT 15:17:53 ON 10 DEC 2001

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L2	233782	S	COLLAGEN
L3	15971	S	NERVE (W) REGENERATION
L4	3929	S	L1 AND L2
L5	69	S	L4 AND L3
L6	18290	S	TYPE (W) I (W) COLLAGEN
L7	5051	S	TYPE (W) III (W) COLLAGEN
L8	11105	S	TYPE (W) IV (W) COLLAGEN
L9	8	S	L5 AND L6
L10	0	S	L5 AND L7
L11	0	S	L5 AND L8
L12	2183	S	L7 AND L6
L13	1542	S	L8 AND L6
L14	3	S	L3 AND L12
L15	3	S	L3 AND L13

=> D L15 IBIB ABS 1-3

L15 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:633122 CAPLUS

DOCUMENT NUMBER: 127:317607

TITLE: Schwann cell extracellular matrix protein production is modulated by Mycobacterium leprae and macrophage secretory products

AUTHOR(S): Singh, Neeta; Birdi, Tannaz J.; Chandrashekar, Sushila; Antia, Noshir H.

CORPORATE SOURCE: The Foundation for Medical Research, 84-A, R.G. Thadani Marg, Worli, Bombay, 400 018, India

SOURCE: J. Neurol. Sci. (1997), 151(1), 13-22
CODEN: JNSCAG; ISSN: 0022-510X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Extracellular matrix (ECM) protein deposition is an important feature of leprous nerves, where Schwann cells (SCs) and macrophages are the main hosts for Mycobacterium leprae. Since, SCs are involved in the synthesis of ECM proteins and its prodn. is regulated by macrophage secretory factors, the present study aimed to det. in vitro, the effect of M. leprae infection and macrophage secretory products on secretion of ECM proteins by SCs in two strains of mice, Swiss White (SW) and C57BL/6, that are known to differ in their nerve pathol. and macrophage functions in response to infection. Following six days of M. leprae infection, SCs from SW mice responded with increased secretion of 14C-leucine radiolabeled proteins and a concomitant increase in laminin and collagens type I, III and IV, as detd. by ELISA. In contrast infected C57BL/6 SCs responded with decreased secretion of total proteins and fibronectin. Exposure of SCs to macrophage conditioned medium resulted in decreased ECM protein secretion in both strains of mice. This decrease was a function of protein breakdown by macrophage derived proteases and also active regulation by macrophage secreted cytokines. A similar effect of M. leprae and macrophage secretory products on SC metab. in leprous nerves would have major ramifications on damage and repair activities. In addn. ECM proteins would also influence the compn. of the infiltrating cell population in lepromatous and tuberculoid nerves.

L15 ANSWER 2 OF 3 MEDLINE

ACCESSION NUMBER: 97369253 MEDLINE
DOCUMENT NUMBER: 97369253 PubMed ID: 9225741
TITLE: Effects of extracellular matrix components on axonal outgrowth from peripheral nerves of adult animals in vitro.
AUTHOR: Tonge D A; Golding J P; Edbladh M; Kroon M; Ekstrom P E; Edstrom A
CORPORATE SOURCE: Physiology Group, King's College, London, United Kingdom.
SOURCE: EXPERIMENTAL NEUROLOGY, (1997 Jul) 146 (1) 81-90. Journal code: EQF; 0370712. ISSN: 0014-4886.
PUB. COUNTRY: United States
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: English
ENTRY MONTH: Priority Journals
ENTRY DATE: 199708
Entered STN: 19970813
Last Updated on STN: 19980206
Entered Medline: 19970807

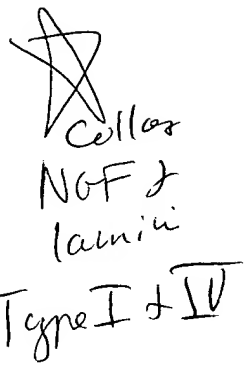
AB Relatively little is known of the growth requirements for regenerating axons of the peripheral nervous system of adult animals. In the present study, we show that extracellular matrix material secreted by the Engelbreth-Holm-Swarm tumor cell line (matrigel) supports axonal growth from explanted peripheral nerve-dorsal root ganglia (DRG) preparations of adult mice and amphibia in serum-free media, without addition of growth factors. Axonal growth in matrigel was much more profuse than that in the more commonly used gels of type 1 collagen and, after some days in culture, was accompanied by migration of Schwann cells along axons. The most abundant protein in matrigel is laminin, which has been shown in many studies to support axonal growth but, surprisingly, antisera to laminin did not inhibit axonal growth in matrigel. To determine the ability of the major components of matrigel, laminin, **type IV collagen**, and heparan sulfate proteoglycan (HSPG), to support axonal growth, these proteins were added to preparations of mouse peripheral nerve-DRGs in **type I collagen** gels. Regenerating axons were significantly longer in the presence of laminin and **type IV collagen** than in control cultures, while HSPG had a slight inhibitory effect. In this assay system, however, diluted matrigel solution was even more effective in stimulating axonal growth than laminin or **type IV collagen**, either alone or in combination. The results suggest that in addition to laminin and **type IV collagen**, other components within matrigel may contribute to its ability to support axonal growth.

Rational for Type IV + laminin in Type I ☆

L15 ANSWER 3 OF 3 MEDLINE
ACCESSION NUMBER: 93208616 MEDLINE
DOCUMENT NUMBER: 93208616 PubMed ID: 8457890
TITLE: Regrowth of motor axons following spinal cord lesions: distribution of laminin and collagen in the CNS scar tissue.
AUTHOR: Risling M; Fried K; Linda H; Carlstedt T; Cullheim S
CORPORATE SOURCE: Department of Anatomy, Karolinska Institutet, Stockholm, Sweden.
SOURCE: BRAIN RESEARCH BULLETIN, (1993) 30 (3-4) 405-14. Journal code: B5M; 7605818. ISSN: 0361-9230.
PUB. COUNTRY: United States
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: English
ENTRY MONTH: Priority Journals
ENTRY DATE: 199304
Entered STN: 19930514
Last Updated on STN: 19930514
Entered Medline: 19930427

AB In previous studies we have demonstrated that spinal motoneurons in the adult cat can regenerate CNS-type axons through CNS scar tissue into denervated ventral roots. This scar tissue, which appears to support and sustain the growth of injured CNS axons, has been shown to have a persistent defect in the blood-brain barrier (BBB). In the present study, the binding of antibodies to nerve growth factor receptor (NGFr), laminin, collagen, and a microtubule associated protein (MAP5) was assessed with

indirect immunohistochemical methods 4 days-20 weeks after a lesion in the ventral funiculus of the spinal cord. An increase in content of collagen-, laminin-, and NGFr-like immunoreactivity was observed in the scar tissue during the first 3 weeks. Although **type I collagen** dominated in superficial areas of the scar, **type IV collagen** and laminin-like immunoreactivity was observed in expanded perivascular spaces all over the lesion zone. **Type IV collagen**- and laminin-immunoreactive structures sometimes appeared to form strands which interconnected the ventral horn and the ventral root. Regenerating axons, as revealed by staining with MAP5 or NGFr antibodies, were observed in close association to these paths. It has been suggested that a breakdown of the BBB may play a vital role in certain types of CNS regeneration by increasing the access of blood-borne trophic factors to the lesion area. The demonstration of extracellular matrix proteins like laminin provides further evidence for the notion that the observed regenerative growth takes place in an environment that is markedly different from the normal CNS.

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     FILE 'BIOSIS, CAPLUS, MEDLINE' ENTERED AT 15:17:53 ON 10 DEC 2001
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L2        233782 S COLLAGEN
L3         15971 S NERVE (W) REGENERATION
L4          3929 S L1 AND L2
L5            69 S L4 AND L3
L6         18290 S TYPE (W) I (W) COLLAGEN
L7          5051 S TYPE (W) III (W) COLLAGEN
L8         11105 S TYPE (W) IV (W) COLLAGEN
L9             8 S L5 AND L6
L10            0 S L5 AND L7
L11            0 S L5 AND L8
L12         2183 S L7 AND L6
L13         1542 S L8 AND L6
L14            3 S L3 AND L12
L15            3 S L3 AND L13

=> S NERVE GROWTH FACTOR
L16       41664 NERVE GROWTH FACTOR

=> S L16 AND L5
L17            5 L16 AND L5

=> D L17 IBIB ABS 1-5

L17  ANSWER 1 OF 5     MEDLINE
ACCESSION NUMBER:    1998417591     MEDLINE
DOCUMENT NUMBER:     98417591   PubMed ID: 9743566
TITLE:               Collagen containing neurotrophin-3 (NT-3)
                     attracts regrowing injured corticospinal axons in the adult
                     rat spinal cord and promotes partial functional recovery.
AUTHOR:              Houweling D A; Lankhorst A J; Gispen W H; Bar P R; Joosten
                     E A
CORPORATE SOURCE:    Department of Neurology, Rudolf Magnus Institute for
                     Neurosciences, Utrecht University, Utrecht, 3508 GA, The
                     Netherlands.
SOURCE:              EXPERIMENTAL NEUROLOGY, (1998 Sep) 153 (1) 49-59.
                     Journal code: EQF; 0370712. ISSN: 0014-4886.
PUB. COUNTRY:        United States
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199810
ENTRY DATE:          Entered STN: 19981029
                     Last Updated on STN: 20000303
                     Entered Medline: 19981019
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AB During development, neurotrophic factors play an important role in the guidance and outgrowth of axons. Our working hypothesis is that neurotrophic factors involved in the development of axons of a particular CNS tract are among the most promising candidates for stimulating and directing the regrowth of fibers of this tract in the lesioned adult animal. The neurotrophin NT-3 is known to be involved in the target selection of outgrowing corticospinal tract (CST) fibers. We studied the capacity of locally applied NT-3 to stimulate and direct the regrowth of axons of the CST in the lesioned adult rat spinal cord. We also studied the effect of NT-3 application on the functional recovery of rats after spinal cord injury, using the gridwalk test. NT-3 was applied at the site of the lesion dissolved into rat tail **collagen** type I. Four weeks after spinal cord injury and **collagen** implantation, significantly more CST fibers had regrown into the **collagen** matrix containing NT-3 (22 +/- 6%, mean +/- SEM) than into the control **collagen** matrix without NT-3 (7 +/- 2%). No CST fibers grew into areas caudal to the **collagen** implant. Despite the absence of regrowth of corticospinal axons into host tissue caudal to the lesion area, functional recovery was observed in rats with NT-3 containing **collagen implants**.

L17 ANSWER 2 OF 5 MEDLINE
ACCESSION NUMBER: 95245754 MEDLINE
DOCUMENT NUMBER: 95245754 PubMed ID: 7728523
TITLE: Axonal growth within poly (2-hydroxyethyl methacrylate) sponges infiltrated with Schwann cells and implanted into the lesioned rat optic tract.
AUTHOR: Plant G W; Harvey A R; Chirila T V
CORPORATE SOURCE: Department of Anatomy and Human Biology, University of Western Australia, Nedlands, Perth.
SOURCE: BRAIN RESEARCH, (1995 Feb 6) 671 (1) 119-30.
Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: English
ENTRY MONTH: Priority Journals
ENTRY DATE: 199506
Entered STN: 19950608
Last Updated on STN: 19950608
Entered Medline: 19950601

AB Porous hydrophilic sponges made from 2-hydroxyethyl methacrylate (HEMA) have a number of possible biomedical applications. We have investigated whether these poly(HEMA) hydrogels, when coated with **collagen** and infiltrated in vitro with cultured Schwann cells, can be implanted into the lesioned optic tract and act as prosthetic bridges to promote axonal regeneration. Nineteen rats (20-21 days old) were given hydrogel/Schwann cell **implants**. No obvious toxic effects were seen, either to the transplanted glia or in the adjacent host tissue. Schwann cells survived the implantation technique and were immunopositive for the low affinity **nerve growth factor** receptor, S100 and laminin. Immunohistochemical studies showed that host non-neuronal cells (astrocytes, oligodendroglia and macrophages) migrated into the implanted hydrogels. Astrocytes were the most frequently observed host cell in the polymer bridges. RT97-positive axons were seen in about two thirds of the **implants**. The axons were closely associated with transplanted Schwann cells and, in some cases, host glia (astrocytes). Individual axons regrowing within the implanted hydrogels could be traced for up to 900 microns, showing that there was continuity in the network of channels within the polymer scaffold. Axons did not appear to be myelinated by either Schwann cells or by migrated host oligodendroglia. In three rats, anterograde tracing with WGA/HRP failed to demonstrate the presence of retinal axons within the hydrogels. The data indicate that poly(HEMA) hydrogels containing Schwann cells have the potential to provide a stable three-dimensional scaffold which is capable of supporting axonal regeneration in the damaged CNS.

L17 ANSWER 3 OF 5 MEDLINE
ACCESSION NUMBER: 93050025 MEDLINE

DOCUMENT NUMBER: 93050025 PubMed ID: 1426123
TITLE: Regeneration of dorsal root axons is related to specific non-neuronal cells lining NGF-treated intraspinal nitrocellulose **implants**.
AUTHOR: Houle J D
CORPORATE SOURCE: Department of Anatomy, University of Arkansas for Medical Sciences, Little Rock 72205.
CONTRACT NUMBER: NS 26380 (NINDS)
SOURCE: EXPERIMENTAL NEUROLOGY, (1992 Nov) 118 (2) 133-42. Journal code: EQF; 0370712. ISSN: 0014-4886.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19980206
Entered Medline: 19921222

AB The regeneration of sensory axons from severed dorsal roots can be enhanced by the presence of **nerve growth factor** (NGF)-treated nitrocellulose strips implanted into an intraspinal lesion cavity. Rather than being directly apposed to the transplant, most regenerating axons are separated from the nitrocellulose by several layers of non-neuronal cells, suggesting that these cells may have a role in the promotion of axonal regrowth. The cellular layers associated with untreated nitrocellulose strips or NGF-treated **implants** were examined in this study to determine if there were differences in their arrangement or orientation along the implant which might explain some of the possible effects of substrate-bound NGF on axonal regrowth. Into a hemisection lesion cavity created in the adult rat lumbar spinal cord NGF-treated or untreated strips of nitrocellulose were placed vertically, with intact pieces of fetal spinal cord (FSC) tissue transplanted along each side. The distal ends of cut dorsal rootlets were apposed to the fetal tissue. Immunocytochemical and electron microscopic examination 30-60 days post-transplantation revealed a distinct layering of cell types along the NGF-treated strips. Closest to the nitrocellulose was a single layer of macrophages, followed by a separate layer of fibroblasts with dense **collagen** bundles, then a layer of astroglial cells, before reaching the neuropil of the fetal spinal cord tissue. A thickened basal lamina formed between the fibroblast and astrocytic cell layers and bundles of regenerated sensory axons extended along the interface between these two layers. In contrast, non-neuronal cells along untreated nitrocellulose strips were not as well organized, with an intermixing of fibroblasts and astroglial cells and only scattered macrophage-like cells. Axons rarely were found in conjunction with this mixed population of cells and, overall, fewer regenerated axons extended into transplants with untreated nitrocellulose. The results demonstrate consistent differences in the composition and organization of non-neuronal cells adjacent to NGF-treated nitrocellulose **implants**, compared to untreated **implants**. This suggests that the presence of bound NGF influences the recruitment of various cells from the surrounding transplant tissue as well as from the previously injured dorsal rootlets. The capacity for NGF to promote the regeneration of sensory axons may be an indirect effect that is mediated or potentiated by the non-neuronal cell population that gathers in response to the presence of bound NGF.

NGF

L17 ANSWER 4 OF 5 MEDLINE
ACCESSION NUMBER: 90187226 MEDLINE
DOCUMENT NUMBER: 90187226 PubMed ID: 1690226
TITLE: Implantation of cultured sensory neurons and Schwann cells into lesioned neonatal rat spinal cord. II. Implant characteristics and examination of corticospinal tract growth.
AUTHOR: Kuhlengel K R; Bunge M B; Bunge R P; Burton H
CORPORATE SOURCE: Department of Anatomy and Neurobiology, Washington University School of Medicine, St. Louis, Missouri 63110.
CONTRACT NUMBER: NS 09809 (NINDS)
NS 09923 (NINDS)
NS 15070 (NINDS)

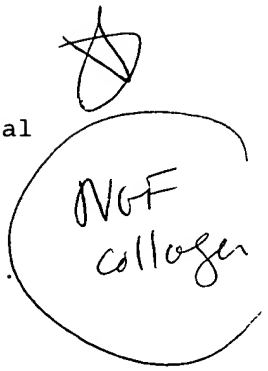
SOURCE: JOURNAL OF COMPARATIVE NEUROLOGY, (1990 Mar 1) 293 (1) 74-91.
Journal code: HUV; 0406041. ISSN: 0021-9967.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199004
ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 19960129
Entered Medline: 19900416

AB The purpose of this study was to test the effectiveness of **implants** derived from peripheral neural tissue to serve as bridges following interruption of the developing corticospinal tract (CST). **Implants** prepared from purified populations of cultured dorsal root ganglion neurons (DRGNs) and Schwann cells (SCs) (Kuhlengel et al., J. Comp. Neurol. 293:63-73, 1990) were placed into thoracolumbar regions of neonatal rat spinal cord from which a 2-mm length of dorsal columns had been removed by suction. These cords were examined by a number of techniques 10 days to 6 months later. The **implants**, recognizable by their DRGN content, filled the vacated dorsal columns and survived the longest periods examined. The most effective method to maintain implant position was dorsal placement of **collagen**-coated Nitex filter. **Implants** were inserted either at the time of lesioning or 5 days later. The implant survival rate was better (72% vs. 50%) and meningeal scarring was less with immediate implantation, but delayed implantation resulted in better implant-cord fusion and the implant better filled the lesion cavity. DRGN/SC **implants** became well vascularized without leptomeningeal cells; this may explain why implant survival was not improved with leptomeningeal cell addition. Particularly well-differentiated **implants** (full extracellular matrix production and myelination) did not fuse as well with cord as did those less well differentiated. The addition of **nerve growth factor** to the Nitex filter **collagen** coating led to improved survival of DRGNs in **implants**. Electron microscopy showed that astrocytes populated the implant-cord junction region and migrated into **implants**. Typical SCs related to nonmyelinated and myelinated axons were present in **implants**. Close proximity of astrocytes and central myelin to SCs and peripheral myelin demonstrated good implant integration with cord. Clusters of SCs, astrocytes, and axons, all enclosed within a common basal lamina, were observed in **implants**. Immunostaining for GFAP and laminin confirmed our microscopy findings that SCs did not migrate from implant into host but that astrocytes left host tissue to enter **implants**. Neuroanatomical tracing of CST neurons with HRP-WGA showed that labeled fibers were not present in the implant but were fasciculated just beneath in gray matter. These fibers remained clustered in gray matter underneath the ventral dorsal columns caudal to the lesion. In lesioned but not implanted rats, labeled fibers were only diffusely distributed in gray matter. Delayed implantation led to more variation in fasciculation compared with immediate implantation.(ABSTRACT TRUNCATED AT 400 WORDS)

L17 ANSWER 5 OF 5 MEDLINE
ACCESSION NUMBER: 90149401 MEDLINE
DOCUMENT NUMBER: 90149401 PubMed ID: 2620177
TITLE: Addition of **nerve growth factor** to the interior of a tubular prosthesis increases sensory neuron regeneration in vivo.
AUTHOR: Da-Silva C F; Langone F
CORPORATE SOURCE: Departamento de Anatomia, Universidade de Sao Paulo, Brasil.
SOURCE: BRAZILIAN JOURNAL OF MEDICAL AND BIOLOGICAL RESEARCH, (1989) 22 (6) 691-4.
Journal code: BOF; 8112917. ISSN: 0100-879X.
PUB. COUNTRY: Brazil
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199003

ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 19980206
Entered Medline: 19900326

AB The sciatic nerve of adult mice was transected and the proximal and distal nerve stumps were sutured into a polyethylene tube. The tubes were implanted either empty, or the lumen was filled with pure **collagen** or a mixture of **collagen/nerve growth factor** (NGF). Six weeks later, cells in the L3-L5 dorsal root ganglia (DRG) were retrogradely filled with horseradish peroxidase (HRP). The data demonstrate that the addition of NGF to the interior of the tubular prosthesis can significantly increase the regeneration rate of sensory neurons.



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L17            5 S L16 AND L5
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L18 33671 LAMININ

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L19 18 L18 AND L5

=> D L19 IBIB ABS 1-18

L19 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:4624 CAPLUS
DOCUMENT NUMBER: 135:200222
TITLE: Bioartificial peripheral nerve guide tube
AUTHOR(S): Shimizu, Ysuhiko
CORPORATE SOURCE: Institute of Medical Science, Kyoto University, Japan
SOURCE: Igaku no Ayumi (2000), 195(3), 184-187
CODEN: IGAYAY; ISSN: 0039-2359
PUBLISHER: Ishiyaku Shuppan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review with 7 refs. on artificial peripheral nerve guide tubes, covering characteristics of gelatin, **collagen**, **collagen**/polyglycolic acid composite, and **laminin**-coated **collagen**/polyglycolic acid composite nerve guide tubes.

L19 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:422742 CAPLUS
DOCUMENT NUMBER: 133:155335

TITLE: Peripheral **nerve regeneration** using silicone rubber chambers filled with **collagen**, **laminin** and fibronectin

AUTHOR(S): Chen, Yueh-Sheng; Hsieh, Ching-Liang; Tsai, Chin-Chuan; Chen, Ter-Hsin; Cheng, Wen-Chiang; Hu, Cheng-Li; Yao, Chun-Hsu

CORPORATE SOURCE: Institute of Chinese Medical Science, China Medical College, Taichung, Taiwan

SOURCE: Biomaterials (2000), 21(15), 1541-1547
CODEN: BIMADU; ISSN: 0142-9612

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A 10 mm gap of rat sciatic nerve was created between the proximal and distal nerve stumps, which were sutured into silicone rubber tubes filled with an extracellular gel contg. **collagen**, **laminin** and fibronectin. Empty silicone rubber tubes were used as controls. Six weeks after implantation, all extracellular elements were completely degraded and absorbed, and 90% of the animals from the extracellular gel group exhibited regeneration across the nerve gaps, whereas only 60% in the control group. Both qual. and quant. histol. of the regenerated nerves revealed a more mature ultrastructural organization with 28% larger cross-sectional area and 28% higher no. of myelinated axons in the extracellular gel group than the controls. The gel mixt. of **collagen**, **laminin** and fibronectin could offer a suitable growth medium for the regeneration of axons.

REFERENCE COUNT: 41

REFERENCE(S):
(2) Aldini, N; Biomaterials 1996, V17, P959 CAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 18 CAPLUS

ACCESSION NUMBER: 2000:400378 CAPLUS

DOCUMENT NUMBER: 133:155361

TITLE: Peripheral **nerve regeneration** across an 80-mm gap bridged by a polyglycolic acid (PGA)-**collagen** tube filled with **laminin**-coated **collagen** fibers: a histological and electrophysiological evaluation of regenerated nerves

AUTHOR(S): Matsumoto, K.; Ohnishi, K.; Kiyotani, T.; Sekine, T.; Ueda, H.; Nakamura, T.; Endo, K.; Shimizu, Y.

CORPORATE SOURCE: Institute for Frontier Medical Sciences, Department of Bioartificial Organs, Kyoto University, Kyoto, 606-8507, Japan

SOURCE: Brain Res. (2000), 868(2), 315-328
CODEN: BRREAP; ISSN: 0006-8993

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We evaluated peripheral **nerve regeneration** across an 80-mm gap using a novel artificial nerve conduit. The conduit was made of a polyglycolic acid (PGA)-**collagen** tube filled with **laminin**-coated **collagen** fibers. Twelve beagle dogs underwent implantation of the nerve conduit across an 80-mm gap in the left peroneal nerve. In 4 other dogs used as neg. controls, the nerve was resected and left unconnected. Histol. observation showed that numerous unmyelinated and myelinated nerve fibers, all smaller in diam. and with a thinner myelin sheath than normal nerve fibers, regrew through and beyond the gap 12 mo after implantation. The distribution of the regenerated axonal diams. was different from that of the normal axonal diams. Compd. muscle action potentials, motor evoked potentials, and somatosensory evoked potentials were recorded in most animals 3 mo after implantation.

Peak amplitudes and latencies recovered gradually, which indicating the functional establishment of the nerve connection with the target organs. In addn. to the ordinary electrophysiol. recoveries, potentials with distinct latencies originating from A.alpha., A.delta. and C fibers became distinguishable at the 6th lumbar vertebra following stimulation of the peroneal nerve distal to the gap 12 mo after implantation. The pattern of walking without load was restored to almost normal 10-12 mo after implantation. Neither electrophysiol. nor histol. restoration was obtained in the controls. Our nerve conduit can guide peripheral nerve elongation and lead to favorable functional recovery across a wider nerve gap than previously reported artificial nerve conduits.

REFERENCE COUNT: 35

REFERENCE(S): (2) Archibald, S; J Neurosci 1995, V15, P4109 CAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:192735 CAPLUS

DOCUMENT NUMBER: 131:23475

TITLE: Evaluation of several techniques to modify denatured muscle tissue to obtain a scaffold for peripheral **nerve regeneration**

AUTHOR(S): Meek, Marcel F.; Den Dunnen, Wilfred F. A.; Schakenraad, Jeff M.; Robinson, Peter H.

CORPORATE SOURCE: Center for Artificial Organs, Division of Biomaterials, University of Groningen, Groningen, 9712 KZ, Neth.

SOURCE: Biomaterials (1999), 20(5), 401-408
CODEN: BIMADU; ISSN: 0142-9612

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The aim of this study was to (1) evaluate the effect of several prepn. techniques of denatured muscle tissue to obtain an open 3-dimensional structure, and (2) test if this scaffold is suitable for peripheral **nerve regeneration**. Four samples (A-D) of muscle tissue specimens were evaluated using light microscopy, immunohistochem. and cryo-SEM. Sample C showed the most open extracellular matrix, while **collagen** type IV and **laminin** (in the basal lamina) could still be obsd. by immunohistochem. An in vivo pilot study showed that the first signs of functional nerve recovery and axon regeneration could be obsd. after 3 wk of implantation. Thus, sample C has the most open structure and leads to good **nerve regeneration** and functional nerve recovery.

REFERENCE COUNT: 21

REFERENCE(S): (3) Den Dunnen, W; Cells Mater 1996, V6(1-3), P93 CAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:367319 CAPLUS

DOCUMENT NUMBER: 122:230597

TITLE: A synthetic **laminin** peptide is active in peripheral **nerve regeneration** in vivo

AUTHOR(S): Takakuda, Kazuo; Miyairi, Hiroo; Itou, Souichirou; O(hta, Tuyoshi; Samejima, Hirotake

CORPORATE SOURCE: Inst. Med. Dent. Eng., Tokyo Med. Dent. Univ., Tokyo,

SOURCE: 101, Japan
Iyo Kizai Kenkyusho Hokoku (Tokyo Ika Shika Daigaku) (1994), 28, 70-4
CODEN: IKKHBS; ISSN: 0082-4739
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB The activity of synthetic **laminin** peptides, which contain YIGSR or IKVAV sequences, were examd. in a **nerve regeneration** model in vivo. A segment of a rat sciatic nerve was replaced by a 15 mm long silicone tube filled with either **collagen** gel, **laminin**-contg. **collagen** gel, **laminin**- and YIGSR peptide-contg. **collagen** gel, YIGSR peptide-contg. **collagen** gel, **laminin** and IKVAV peptide-contg. **collagen** gel, or IKVAV peptide-contg. **collagen** gel. At 2, 4, 6, 8, and 10 wk after surgery, the **implants** were retrieved and histol. examd. by light and electron microscopy. Many regenerated axons were found in the tubes filled with the **laminin**-contg. **collagen** gel, whereas none in the ones with **collagen** gel alone. When the YIGSR peptide was applied with **laminin**, it inhibited **nerve regeneration**; however, without **laminin**, it enhanced regeneration. The IKVAV peptide showed no inhibitory or enhancing effects. The authors concluded that the main functional domain of **laminin** in **nerve regeneration** is the YIGSR sequence, and this synthetic peptide may be used as a growth guidance agent in neural prostheses.

Collagen Laminin ?

L19 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1987:605246 CAPLUS
DOCUMENT NUMBER: 107:205246
TITLE: High molecular weight bioresorbable polymers and implantation devices, especially for promotion of nerve growth
INVENTOR(S): Mares, Frank; Tang, Reginald Ting Hong; Chiu, Tin Ho; Largman, Theodore
PATENT ASSIGNEE(S): Allied Corp., USA
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 226061	A2	19870624	EP 1986-116047	19861120
EP 226061	A3	19880720		
EP 226061	B1	19940216		
R: CH, DE, GB, LI				
JP 62144663	A2	19870627	JP 1986-298597	19861215
JP 05052749	B4	19930806		

PRIORITY APPLN. INFO.: US 1985-809978 19851217

AB Prosthetic **implants** for encouraging cellular growth and regeneration of function, esp. for nerve tissue, consist of a bioresorbable polymer (mol. wt. .gtoreq.150,000). Mouse sciatic nerves (from 3 individuals) were severed and the ends were sutured and inserted into a 5-6 mm nerve guide tube of the invention (DL-lactic acid homopolymer) to give a gap of 3-4 mm. The no. of myelinated axons, detd. by computer, was 1457 .+-. 124 and 1844 .+-. 429 after 4 wks and 6 wks, resp., for a polymer with mol. wt. 234,000.

L19 ANSWER 7 OF 18 MEDLINE
ACCESSION NUMBER: 2000492373 MEDLINE
DOCUMENT NUMBER: 20340235 PubMed ID: 10885726
TITLE: Peripheral **nerve regeneration** using silicone rubber chambers filled with **collagen**, **laminin** and fibronectin.
AUTHOR: Chen Y S; Hsieh C L; Tsai C C; Chen T H; Cheng W C; Hu C L; Yao C H
CORPORATE SOURCE: Institute of Chinese Medical Science, China Medical

Collagen Laminin

SOURCE: College, Taichung, Taiwan, ROC.
BIOMATERIALS, (2000 Aug) 21 (15) 1541-7.
PUB. COUNTRY: Journal code: A4P; 8100316. ISSN: 0142-9612.
ENGLAND: United Kingdom
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: English
ENTRY MONTH: Priority Journals
ENTRY DATE: 200010
Entered STN: 20001027
Last Updated on STN: 20001027
Entered Medline: 20001013

AB A 10 mm gap of rat sciatic nerve was created between the proximal and distal nerve stumps, which were sutured into silicone rubber tubes filled with an extracellular gel containing **collagen**, **laminin** and fibronectin. Empty silicone rubber tubes were used as controls. Six weeks after implantation, all extracellular elements were completely degraded and absorbed, and 90% of the animals from the extracellular gel group exhibited regeneration across the nerve gaps, whereas only 60% in the control group. Both qualitative and quantitative histology of the regenerated nerves revealed a more mature ultrastructural organization with 28% larger cross-sectional area and 28% higher number of myelinated axons in the extracellular gel group than the controls. These results showed that the gel mixture of **collagen**, **laminin** and fibronectin could offer a suitable growth medium for the regeneration of axons.

L19 ANSWER 8 OF 18 MEDLINE
ACCESSION NUMBER: 2000401895 MEDLINE
DOCUMENT NUMBER: 20314261 PubMed ID: 10854584
TITLE: Peripheral **nerve regeneration** across an 80-mm gap bridged by a polyglycolic acid (PGA)-**collagen** tube filled with **laminin**-coated **collagen** fibers: a histological and electrophysiological evaluation of regenerated nerves.
AUTHOR: Matsumoto K; Ohnishi K; Kiyotani T; Sekine T; Ueda H; Nakamura T; Endo K; Shimizu Y
CORPORATE SOURCE: Department of Bioartificial Organs, Institute for Frontier Medical Sciences, Kyoto University, Kawahara-cho 53, Shogoin Sakyo-ku, 606-8507, Kyoto, Japan..
matumoto@frontier.kyoto-u.ac.jp
SOURCE: BRAIN RESEARCH, (2000 Jun 23) 868 (2) 315-28.
PUB. COUNTRY: Journal code: B5L; 0045503. ISSN: 0006-8993.
Netherlands
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: English
ENTRY MONTH: Priority Journals
ENTRY DATE: 200008
Entered STN: 20000901
Last Updated on STN: 20000901
Entered Medline: 20000818

AB We evaluated peripheral **nerve regeneration** across an 80-mm gap using a novel artificial nerve conduit. The conduit was made of a polyglycolic acid (PGA)-**collagen** tube filled with **laminin**-coated **collagen** fibers. Twelve beagle dogs underwent implantation of the nerve conduit across an 80-mm gap in the left peroneal nerve. In four other dogs used as negative controls, the nerve was resected and left unconnected. Histological observation showed that numerous unmyelinated and myelinated nerve fibers, all smaller in diameter and with a thinner myelin sheath than normal nerve fibers, regrew through and beyond the gap 12 months after implantation. The distribution of the regenerated axonal diameters was different from that of the normal axonal diameters. Compound muscle action potentials, motor evoked potentials, and somatosensory evoked potentials were recorded in most animals 3 months after implantation. Peak amplitudes and latencies recovered gradually, which indicating the functional establishment of the nerve connection with the target organs. In addition to the ordinary electrophysiological recoveries, potentials with distinct latencies originating from Aalpha, Adelta and C fibers became distinguishable at the 6th lumbar vertebra following stimulation of the peroneal nerve distal to

the gap 12 months after implantation. The pattern of walking without load was restored to almost normal 10-12 months after implantation. Neither electrophysiological nor histological restoration was obtained in the controls. Our nerve conduit can guide peripheral nerve elongation and lead to favorable functional recovery across a wider nerve gap than previously reported artificial nerve conduits.

L19 ANSWER 9 OF 18 MEDLINE
ACCESSION NUMBER: 1999229701 MEDLINE
DOCUMENT NUMBER: 99229701 PubMed ID: 10214888
TITLE: Functional recovery following nerve injury and repair by silicon tubulization: comparison of **laminin** -fibronectin, dialyzed plasma, **collagen** gel, and phosphate buffered solution.
AUTHOR: Terris D J; Cheng E T; Utley D S; Tarn D M; Ho P R; Verity A N
CORPORATE SOURCE: Stanford University Medical Center, Division of Otolaryngology/Head and Neck Surgery, CA 94305-5328, USA.. dterris@stanford.edu
SOURCE: AURIS, NASUS, LARYNX, (1999 Apr) 26 (2) 117-22. Journal code: 9FZ; 7708170. ISSN: 0385-8146.
PUB. COUNTRY: Netherlands
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: English
ENTRY MONTH: Priority Journals
ENTRY DATE: 199907
Entered STN: 19990806
Last Updated on STN: 19990806
Entered Medline: 19990728

AB PURPOSE: This study was designed to investigate the potential for enhancement of peripheral **nerve regeneration** by the manipulation of the neural microenvironment with **laminin** -fibronectin solution (LF), dialyzed plasma (DP), **collagen** gel (CG), or phosphate buffered saline (PBS) in a silicon tubulization repair model. METHOD: A rat sciatic nerve model of injury and repair was used to study the effects of exogenous matrix precursors (contained in LF or DP), CG or PBS on **nerve regeneration**. A total of 50 Sprague-Dawley rats underwent left sciatic nerve transection and repair by silicon tubulization. The silicon tubules were either left empty (E), or filled with solutions of LF, DP, CG, or PBS. Nerve function was assessed preoperatively and then postoperatively, every 10 days for 90 days using sciatic functional indexes (SFI). On postoperative day 90, the sciatic nerves were harvested for histologic analysis and the posterior compartment muscles of each animal were harvested and weighed. Molecular analysis for two proteins associated with neural regeneration was performed on the nerve segments. RESULTS: All five animal groups demonstrated equivalent functional recovery. Comparison of the rate of recovery and mean maximal recovery between each group revealed no statistically significant differences, with P-values ranging from 0.30 to 0.95. Posterior compartment muscle masses were similar in all groups except for LF, whose animals had muscle masses 8-9% lower than CG, PBS, or E ($P < 0.05$). CONCLUSION: Alteration of the regenerating neural microenvironment with exogenous matrix precursors (LF, DP), CG or PBS failed to improve sciatic functional recovery after nerve transection and silicon tubulization in this model. From this study, we conclude that LF, DP, CG, and PBS do not enhance the rate or degree of recovery of peripheral nerve function across a narrow gap when nerves are repaired by silicon tubulization.

L19 ANSWER 10 OF 18 MEDLINE
ACCESSION NUMBER: 1998374081 MEDLINE
DOCUMENT NUMBER: 98374081 PubMed ID: 9710307
TITLE: Implantation of **collagen** IV/poly(2-hydroxyethyl methacrylate) hydrogels containing Schwann cells into the lesioned rat optic tract.
AUTHOR: Plant G W; Chirila T V; Harvey A R
CORPORATE SOURCE: Department of Anatomy and Human Biology, The University of Western Australia, Perth, Australia.
SOURCE: CELL TRANSPLANTATION, (1998 Jul-Aug) 7 (4) 381-91.

Journal code: B02; 9208854. ISSN: 0963-6897.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981028

AB Poly (2-hydroxyethylmethacrylate) (PolyHEMA) hydrogels, when combined with extracellular matrix molecules and infiltrated with cultured Schwann cells, have the capability to induce CNS axonal regrowth after injury. We have further investigated these PolyHEMA hydrogels and their potential to bridge CNS injury sites. **Collagen** IV-impregnated hydrogels containing Schwann cells were implanted into the lesioned optic tract in 14 rats. On examination 2-4 months later, there was good adherence between the **implants** and CNS tissue, and large numbers of viable Schwann cells (S100+, GFAP+, **Laminin**+, and LNGFR+) were seen within the hydrogel matrices. Immunohistochemical analysis showed that the **collagen** IV-impregnated PolyHEMA hydrogels preferentially supported the transplanted Schwann cells and not host glial cells such as astrocytes (GFAP+) or oligodendroglia (CAII+). Macrophages (ED1+) were also seen within the sponge structure. Eighty-three percent of the implanted hydrogels contained RT97+ axons within their trabecular networks. Regrowing axons were associated with the transplanted Schwann cells and not with the small number of infiltrating astrocytes. RT97+ axons were traced up to 510 microm from the nearest host neuropil. These axons were sometimes myelinated by the transplanted Schwann cells and expressed the peripheral myelin marker Po+. WGA/HRP-labeled retinal axons were seen within transplanted hydrogel sponges, with 40% of the cases growing for distances up to 350-450 microm within the polymer network. The data indicate that impregnating PolyHEMA sponges with **collagen** IV can modify the host glial reaction and support the survival of transplanted Schwann cells. This study thus provides new information on how biomaterials could be used to modify and bridge CNS injury sites.

IV

L19 ANSWER 11 OF 18 MEDLINE
ACCESSION NUMBER: 96349812 MEDLINE
DOCUMENT NUMBER: 96349812 PubMed ID: 8741371
TITLE: Peripheral **nerve regeneration** in a silicone tube: effect of **collagen** sponge prosthesis, **laminin**, and pyrimidine compound administration.
AUTHOR: Ohbayashi K; Inoue H K; Awaya A; Kobayashi S; Kohga H; Nakamura M; Ohye C
CORPORATE SOURCE: Department of Neurosurgery, Gunma University School of Medicine, Maebashi.
SOURCE: NEUROLOGIA MEDICO-CHIRURGICA, (1996 Jul) 36 (7) 428-33.
Journal code: NYD; 0400775. ISSN: 0470-8105.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961106
Last Updated on STN: 19980206
Entered Medline: 19961023

AB Regeneration of transected peripheral nerve with a 10-mm gap encased in a silicone tube was evaluated in the presence of **collagen** sponge with or without **laminin**, or with systemic administration of a pyrimidine compound, MS-818. The sciatic nerve of 20 adult rats was transected and the proximal and distal nerve stumps were fixed in a silicone tube. The lumen of the silicone tube was empty, or filled with a **collagen** sponge alone or with a **laminin**-soaked **collagen** sponge. Also, a pyrimidine compound was injected intraperitoneally after implantation of the empty silicone tube. Three weeks later, the contents of the silicone tubes were processed for histological examination of regenerated nerve fibers. Other animals were observed 6, 12, and 18 months after surgery to examine the long-term

effects of the **collagen** sponge on **nerve regeneration**. All animals had regenerated tissue within the tube 3 weeks after nerve transection. The diameter of the tissue decreased toward the distal stump in the empty tube, but was the same throughout the full length in the **collagen** sponge-containing tube. Immunohistochemical studies revealed that the nerve fibers extended beyond the midline of the regenerated tissue in animals treated with a **laminin**-containing **collagen** sponge or receiving a pyrimidine compound. Long-term observation showed the regenerated nerve was thick as the proximal stump and many neurofilament- and peripheral myelin-positive fibers were observed around the **collagen** sponge. **Collagen** sponge assists the progress of regenerated tissues in silicone tubes, and **laminin**-containing prostheses and administration of a pyrimidine compound enhance peripheral **nerve regeneration**.

L19 ANSWER 12 OF 18 MEDLINE
ACCESSION NUMBER: 95245754 MEDLINE
DOCUMENT NUMBER: 95245754 PubMed ID: 7728523
TITLE: Axonal growth within poly (2-hydroxyethyl methacrylate) sponges infiltrated with Schwann cells and implanted into the lesioned rat optic tract.
AUTHOR: Plant G W; Harvey A R; Chirila T V
CORPORATE SOURCE: Department of Anatomy and Human Biology, University of Western Australia, Nedlands, Perth.
SOURCE: BRAIN RESEARCH, (1995 Feb 6) 671 (1) 119-30.
Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: English
ENTRY MONTH: Priority Journals
ENTRY DATE: 199506
Entered STN: 19950608
Last Updated on STN: 19950608
Entered Medline: 19950601

AB Porous hydrophilic sponges made from 2-hydroxyethyl methacrylate (HEMA) have a number of possible biomedical applications. We have investigated whether these poly(HEMA) hydrogels, when coated with **collagen** and infiltrated in vitro with cultured Schwann cells, can be implanted into the lesioned optic tract and act as prosthetic bridges to promote axonal regeneration. Nineteen rats (20-21 days old) were given hydrogel/Schwann cell **implants**. No obvious toxic effects were seen, either to the transplanted glia or in the adjacent host tissue. Schwann cells survived the implantation technique and were immunopositive for the low affinity nerve growth factor receptor, S100 and **laminin**. Immunohistochemical studies showed that host non-neuronal cells (astrocytes, oligodendroglia and macrophages) migrated into the implanted hydrogels. Astrocytes were the most frequently observed host cell in the polymer bridges. RT97-positive axons were seen in about two thirds of the **implants**. The axons were closely associated with transplanted Schwann cells and, in some cases, host glia (astrocytes). Individual axons regrowing within the implanted hydrogels could be traced for up to 900 microns, showing that there was continuity in the network of channels within the polymer scaffold. Axons did not appear to be myelinated by either Schwann cells or by migrated host oligodendroglia. In three rats, anterograde tracing with WGA/HRP failed to demonstrate the presence of retinal axons within the hydrogels. The data indicate that poly(HEMA) hydrogels containing Schwann cells have the potential to provide a stable three-dimensional scaffold which is capable of supporting axonal regeneration in the damaged CNS.

L19 ANSWER 13 OF 18 MEDLINE
ACCESSION NUMBER: 95153321 MEDLINE
DOCUMENT NUMBER: 95153321 PubMed ID: 7850464
TITLE: Sciatic **nerve regeneration** navigated by **laminin**-fibronectin double coated biodegradable **collagen** grafts in rats.
AUTHOR: Tong X J; Hirai K; Shimada H; Mizutani Y; Izumi T; Toda N; Yu P

CORPORATE SOURCE: Department of Anatomy, Kanazawa Medical University, Ishikawa, Japan.
SOURCE: BRAIN RESEARCH, (1994 Nov 7) 663 (1) 155-62.
Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950322
Last Updated on STN: 19950322
Entered Medline: 19950314

AB Biodegradable type I **collagen** tube grafts filled longitudinally with **laminin** and fibronectin double coated **collagen** fiber bundles (L-F grafts) were implanted to promote sciatic **nerve regeneration** in rats. Grafts filled with uncoated **collagen** fibers were used as control. A 1 cm defect on the right sciatic nerve was filled with a graft in the manner of bridging. Thirty days after implantation, several newly developed nerve fasciculi were found at the middle portion of the L-F grafts in contrast to no developed nerves in the controls. After 60 days, the middle and distal portions of both grafts included well-developed nerve tissues with prominent myelinated and unmyelinated nerve fibers surrounded by perineural cells, but the control distal portion showed fewer nerve fibers. All artificial **collagen** elements were completely degraded and absorbed at 30 days, and new nerve tissues surrounded by an epineurium successfully connected the proximal stump to the distal stump of the initially separated nerve. Descending and ascending action potentials were evoked in all grafts at 60 days. These results indicated that **laminin** and fibronectin may promote the growth of axons in biodegradable **collagen** grafts, which guided **nerve regeneration** well and allowed the formation of epineurium.

L19 ANSWER 14 OF 18 MEDLINE
ACCESSION NUMBER: 90187226 MEDLINE
DOCUMENT NUMBER: 90187226 PubMed ID: 1690226
TITLE: Implantation of cultured sensory neurons and Schwann cells into lesioned neonatal rat spinal cord. II. Implant characteristics and examination of corticospinal tract growth.
AUTHOR: Kuhlengel K R; Bunge M B; Bunge R P; Burton H
CORPORATE SOURCE: Department of Anatomy and Neurobiology, Washington University School of Medicine, St. Louis, Missouri 63110.
CONTRACT NUMBER: NS 09809 (NINDS)
NS 09923 (NINDS)
NS 15070 (NINDS)
SOURCE: JOURNAL OF COMPARATIVE NEUROLOGY, (1990 Mar 1) 293 (1) 74-91.
Journal code: HUV; 0406041. ISSN: 0021-9967.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199004
ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 19960129
Entered Medline: 19900416

AB The purpose of this study was to test the effectiveness of **implants** derived from peripheral neural tissue to serve as bridges following interruption of the developing corticospinal tract (CST). **Implants** prepared from purified populations of cultured dorsal root ganglion neurons (DRGNs) and Schwann cells (SCs) (Kuhlengel et al., J. Comp. Neurol. 293:63-73, 1990) were placed into thoracolumbar regions of neonatal rat spinal cord from which a 2-mm length of dorsal columns had been removed by suction. These cords were examined by a number of techniques 10 days to 6 months later. The **implants**, recognizable by their DRGN content, filled the vacated dorsal columns and survived the longest periods examined. The most effective method to maintain implant position was dorsal placement of **collagen**-coated Nitex filter.

Implants were inserted either at the time of lesioning or 5 days later. The implant survival rate was better (72% vs. 50%) and meningeal scarring was less with immediate implantation, but delayed implantation resulted in better implant-cord fusion and the implant better filled the lesion cavity. DRGN/SC **implants** became well vascularized without leptomeningeal cells; this may explain why implant survival was not improved with leptomeningeal cell addition. Particularly well-differentiated **implants** (full extracellular matrix production and myelination) did not fuse as well with cord as did those less well differentiated. The addition of nerve growth factor to the Nitex filter **collagen** coating led to improved survival of DRGNs in **implants**. Electron microscopy showed that astrocytes populated the implant-cord junction region and migrated into **implants**. Typical SCs related to nonmyelinated and myelinated axons were present in **implants**. Close proximity of astrocytes and central myelin to SCs and peripheral myelin demonstrated good implant integration with cord. Clusters of SCs, astrocytes, and axons, all enclosed within a common basal lamina, were observed in **implants**. Immunostaining for GFAP and **laminin** confirmed our microscopy findings that SCs did not migrate from implant into host but that astrocytes left host tissue to enter **implants**. Neuroanatomical tracing of CST neurons with HRP-WGA showed that labeled fibers were not present in the implant but were fasciculated just beneath in gray matter. These fibers remained clustered in gray matter underneath the ventral dorsal columns caudal to the lesion. In lesioned but not implanted rats, labeled fibers were only diffusely distributed in gray matter. Delayed implantation led to more variation in fasciculation compared with immediate implantation.(ABSTRACT TRUNCATED AT 400 WORDS)

L19 ANSWER 15 OF 18 MEDLINE
ACCESSION NUMBER: 89157194 MEDLINE
DOCUMENT NUMBER: 89157194 PubMed ID: 2921658
TITLE: Effect of different surgical repair modalities on regeneration of the rabbit mandibular nerve.
AUTHOR: Eppley B L; Doucet M J; Winkelmann T; Delfino J J
CORPORATE SOURCE: Division of Oral-Maxillofacial Surgery, St John's Mercy Medical Center, St Louis, MO 63141.
SOURCE: JOURNAL OF ORAL AND MAXILLOFACIAL SURGERY, (1989 Mar) 47 (3) 257-76.
Journal code: JIC; 8206428. ISSN: 0278-2391.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Dental Journals; Priority Journals
ENTRY MONTH: 198904
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19980206
Entered Medline: 19890407

AB A study was designed to evaluate the ability of the rabbit mandibular nerve to regenerate when exposed to crush and resection injuries, as well as to determine how differently sized resection injuries healed when repaired with either autogenous grafts or **laminin**-lined **collagen** tubulization. The nerve demonstrated a regenerative capacity over a 1-cm defect, with morphology and function that approximated normals, but could not span a 2-cm gap defect unaided. Crush injuries produced findings that were inferior to both those in normal nerves and in those with resections. In 1-cm defects, both grafting and tubular repairs produced similar results, with substantial recovery of neural function after 16 weeks. In 2-cm defects, autogenous grafting was superior to tubulization by both morphologic and functional assessment. Replacement of the lateral cortex of the mandible after nerve repair was shown to be unnecessary. The implications of these findings as they relate to nerve injury and repair in humans is discussed.

L19 ANSWER 16 OF 18 MEDLINE
ACCESSION NUMBER: 89099434 MEDLINE
DOCUMENT NUMBER: 89099434 PubMed ID: 2911622
TITLE: Exogenous **laminin** induces regenerative changes in

traumatized sciatic and optic nerve.
AUTHOR: Politis M J
CORPORATE SOURCE: Department of Orthopedic Surgery, Shaughnessy Research Centre, Vancouver, British Columbia, Canada.
SOURCE: PLASTIC AND RECONSTRUCTIVE SURGERY, (1989 Feb) 83 (2) 228-35.
Journal code: P9S; 1306050. ISSN: 0032-1052.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198902
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19890223

AB **Laminin** is an extracellular matrix component which can promote neuritic elongation in vitro and has been implicated in the promotion of **nerve regeneration** in vivo. The present study was undertaken to determine if implantation of Elvax pellets containing exogenous **laminin** distal to site of lesion could promote regenerative responses in vivo in the adult rat peripheral (sciatic) and central (optic) nerve. In peripheral nerve preparations, Elvax pellets containing **laminin** or **collagen** were assessed for their ability to "lure" transected axons into 5-mm-long silicone tubes. In optic nerve studies, **laminin** pellets were inserted distal to site of nerve crush, and the extent of axonal elongation 2.5 mm to the injury site was assessed. **Laminin**-containing pellets appeared to support appreciable axonal elongation in both systems. This effect was dose-dependent and not exerted by **collagen** pellets, substrate-free pellets, or pellets containing irradiated **laminin**. **Collagen** IV had some beneficial effect in peripheral, but not central, nerve preparations.

Col IV

L19 ANSWER 17 OF 18 MEDLINE
ACCESSION NUMBER: 88270052 MEDLINE
DOCUMENT NUMBER: 88270052 PubMed ID: 3390701
TITLE: Entubulation repair with protein additives increases the maximum nerve gap distance successfully bridged with tubular prostheses.
AUTHOR: Madison R D; Da Silva C F; Dikkes P
CORPORATE SOURCE: Department of Neuroscience, Children's Hospital, Boston, MA 02115.
CONTRACT NUMBER: NS22404 (NINDS)
SOURCE: BRAIN RESEARCH, (1988 May 3) 447 (2) 325-34.
Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198808
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19980206
Entered Medline: 19880812

AB The major objective of the experiments reported in this paper was to test the hypothesis that the maximum distance that peripheral nervous system (PNS) axons can regenerate through a tubular prosthesis may be increased by specific modifications to the internal environment of the prosthesis. The sciatic nerve of adult male rats was transected and proximal and distal nerve stumps were sutured into a silicone tube 20-25 mm in length. The silicone tubes were implanted empty, or the lumen was filled with **collagen** or a **laminin**-containing gel. Following 4-16 weeks survival time animals were sacrificed and the contents of the silicone tubes were processed for histological identification of myelinated and unmyelinated axons. All of the tubes with additives, but one of the initially empty tubes, displayed a regenerated nerve cable within the tube. Retrograde labeling studies were carried out to prove that some of the axons present in the regenerated nerve cables arose from primary motor and sensory neurons. These results show that specific modifications to the microenvironment of regenerating PNS axons can affect

the success or failure of tubular prostheses for nerve repair.

L19 ANSWER 18 OF 18 MEDLINE
ACCESSION NUMBER: 87049363 MEDLINE
DOCUMENT NUMBER: 87049363 PubMed ID: 3778752
TITLE: Regeneration of transected sciatic nerves through semi-permeable nerve guidance channels. Effects of extracellular matrix protein additives.
AUTHOR: Aebischer P; Valentini R F; Winn S R; Kunz S; Sasken H; Galletti P M
SOURCE: ASAIO TRANSACTIONS, (1986 Jul-Sep) 32 (1) 474-7. Journal code: ASA; 8611947. ISSN: 0889-7190.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198701
ENTRY DATE: Entered STN: 19900302
Last Updated on STN: 19980206
Entered Medline: 19870112

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(FILE 'HOME' ENTERED AT 15:17:07 ON 10 DEC 2001)

FILE 'BIOSIS, CAPLUS, MEDLINE' ENTERED AT 15:17:53 ON 10 DEC 2001
L1 92198 S IMPLANTS
L2 233782 S COLLAGEN
L3 15971 S NERVE (W) REGENERATION
L4 3929 S L1 AND L2
L5 69 S L4 AND L3
L6 18290 S TYPE (W) I (W) COLLAGEN
L7 5051 S TYPE (W) III (W) COLLAGEN
L8 11105 S TYPE (W) IV (W) COLLAGEN
L9 8 S L5 AND L6
L10 0 S L5 AND L7
L11 0 S L5 AND L8
L12 2183 S L7 AND L6
L13 1542 S L8 AND L6
L14 3 S L3 AND L12
L15 3 S L3 AND L13
L16 41664 S NERVE GROWTH FACTOR
L17 5 S L16 AND L5
L18 33671 S LAMININ
L19 18 S L18 AND L5

=> S PERITONEAL TISSUE
L20 387 PERITONEAL TISSUE

=> S L20 AND L5
L21 0 L20 AND L5

=> S L20 AND L3
L22 0 L20 AND L3

=> S L20 AND L2
L23 18 L20 AND L2

=> S L20 AND L4
L24 0 L20 AND L4

=> D L23 IBIB ABS 1-18

L23 ANSWER 1 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:291656 BIOSIS
DOCUMENT NUMBER: PREV200100291656
TITLE: Dipyridamole inhibits human peritoneal mesothelial cell proliferation in vitro and attenuates rat peritoneal

fibrosis in vivo.
AUTHOR(S): Hung, Kuan-Yu; Shyu, Ren-Shi; Fang, Cheng-Chung; Tsai, Chien-Chen; Lee, Po-Huang; Tsai, Tun-Jun (1); Hsieh, Bor-Shen
CORPORATE SOURCE: (1) Department of Internal Medicine, National Taiwan University Hospital, No. 7, Chung-Shan South Road, Taipei: paul@ha.mc.ntu.edu.tw Taiwan
SOURCE: Kidney International, (June, 2001) Vol. 59, No. 6, pp. 2316-2324. print.
ISSN: 0085-2538.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background: Peritoneal fibrosis (PF) is one of the most serious complications after long-term continuous ambulatory peritoneal dialysis (CAPD). Proliferation of human peritoneal mesothelial cells (HPMC) and matrix over-production are regarded as the main processes predisposing to PF. Dipyridamole (DP) has been reported to have potential as an antiproliferative and antifibrotic agent. We thus investigated the effect of DP in inhibiting proliferation and **collagen** synthesis of HPMC. A rat model of peritonitis-induced PF was also established to demonstrate the in vivo preventive effect of DP. Methods: HPMC was cultured from human omentum by an enzyme digestion method. Cell proliferation was measured by the methyltetrazolium assay. Intracellular cAMP was measured using an enzyme immunoassay (EIA) kit. Total **collagen** synthesis was measured by 3H-proline incorporation assay. Expression of **collagen** alpha1 (I) and **collagen** alpha1 (III) mRNAs was determined by Northern blotting. The rat model of peritonitis-induced PF was developed by adding dextran microbeads (Cytodex, 8 mg/1 mL volume) to a standardized suspension (3 X 109) of Staphylococcus aureus. DP was administrated via intravenous infusion (4 mg in 1 h) daily for seven days. Macroscopic grading of intraperitoneal adhesions and histological analyses of peritoneal thickness and **collagen** expression were performed. Results: Addition of DP to HPMC cultures suppressed serum-stimulated cell proliferation and **collagen** synthesis. The antimitogenic and antifibrotic effects of DP appear to be predominantly mediated through the cAMP pathway, as DP increased intracellular cAMP in a dose-dependent manner. The macroscopic grade of intraperitoneal adhesion and peritoneal thickness were both significantly increased in animals treated with Cytodex plus S. aureus; on the other hand, DP attenuated these fibrotic changes with statistical significance ($P < 0.01$). Analysis of gene expression of **collagen** alpha1 (I) and alpha1 (III) in the **peritoneal tissue** of experimental animals yielded similar results. Conclusions: This study suggests that dipyridamole may have therapeutic potential in treating peritoneal fibrosis.

L23 ANSWER 2 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:494195 BIOSIS
DOCUMENT NUMBER: PREV200000494316
TITLE: Expression of heat shock proteins 47 and 70 in the peritoneum of patients on continuous ambulatory peritoneal dialysis.
AUTHOR(S): Shioshita, Kei; Miyazaki, Masanobu (1); Ozono, Yoshiyuki; Abe, Katsushige; Taura, Kouichi; Harada, Takashi; Koji, Takehiko; Taguchi, Takashi; Kohno, Shigeru
CORPORATE SOURCE: (1) The Second Department of Internal Medicine, Nagasaki University School of Medicine, 1-7-1 Sakamoto, Nagasaki, 852-8521 Japan
SOURCE: Kidney International, (February, 2000) Vol. 57, No. 2, pp. 619-631. print.
ISSN: 0085-2538.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background. Peritoneal sclerosis, characterized by **collagen** accumulation, is a serious complication in continuous ambulatory peritoneal dialysis (CAPD) therapy. Heat shock protein 47 (HSP47) is a **collagen**-specific molecular chaperon and is closely associated

with **collagen** synthesis. Methods. We determined the expression of HSP47 and HSP70 (nonspecific for **collagen** synthesis) by immunohistochemistry in **peritoneal tissues** of patients on CAPD. The tissue for **collagen** III, alpha-smooth muscle actin (alpha-SMA), and CD68 (a marker for macrophages) were also stained. Thirty-two peritoneal samples were divided into three groups (group A1, 11 patients who had no ultrafiltration loss; group A2, 9 patients who had ultrafiltration loss; and group B, 12 specimens who had endstage renal disease prior to induction of CAPD. Results. In group B, staining for HSP47, HSP70, and **collagen** III in **peritoneal tissues** was faint, and only a few cells were positive for alpha-SMA and CD68. In contrast, HSP47, HSP70, and **collagen** III were expressed in areas of thickened connective tissues in fibrotic peritoneal specimens of CAPD patients. The expression level of HSP47, HSP70, **collagen** III, and alpha-SMA and the number of CD68-positive cells in group A2 were significantly higher than those in groups A1 and B. HSP47/HSP70-positive cells were mesothelial cells, adipocytes, and alpha-SMA-positive myofibroblasts. Furthermore, the expression level of HSp47 was significantly higher in peritoneal specimens from patients with refractory peritonitis than without it and was significantly higher in patients with more than 60 months of CAPD therapy than that in patients with less than 60 months of CAPD. Conclusion. Our results indicate that CAPD therapy may induce HSPs in the **peritoneal tissue**, and that peritonitis in CAPD patients may be associated with the progression of peritoneal sclerosis at least through HSP47 expression and chronic macrophage infiltration. Our data also suggest that the progression of peritoneal sclerosis in such patients is associated with deterioration of peritoneal ultrafiltration function.

L23 ANSWER 3 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:526585 BIOSIS
DOCUMENT NUMBER: PREV199900526585
TITLE: Immunohistochemistry (IHC) for heat shock protein 47 (HSP47) expression in **peritoneal tissues** of rats with experimentally induced fibrosis.
AUTHOR(S): Mishima, Yoko (1); Miyazaki, M. (1); Ozono, Y. (1); Shioshita, K. (1); Harada, T. (1); Taguchi, T. (1); Koji, T. (1); Kohno, S. (1)
CORPORATE SOURCE: (1) 2nd Dept of Internal Med, Nagasaki Univ, Nagasaki Japan
SOURCE: Journal of the American Society of Nephrology, (Sept., 1999) Vol. 10, No. PROGRAM AND ABSTR. ISSUE, pp. 318A. Meeting Info.: 32nd Annual Meeting of the American Society of Nephrology Miami Beach, Florida, USA November 1-8, 1999 American Society of Nephrology . ISSN: 1046-6673.
DOCUMENT TYPE: Conference
LANGUAGE: English

L23 ANSWER 4 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:224553 BIOSIS
DOCUMENT NUMBER: PREV199900224553
TITLE: Coelomic metaplasia theory of endometriosis: Evidence from in vivo studies and an in vitro experimental model.
AUTHOR(S): Matsuura, Kohei (1); Ohtake, Hideyuki; Katabuchi, Hidetaka; Okamura, Hitoshi
CORPORATE SOURCE: (1) Department of Obstetrics and Gynecology, Kumamoto University School of Medicine, Honjo 1-1-1, Kumamoto, 860-8556 Japan
SOURCE: Gynecologic and Obstetric Investigation, (March, 1999) Vol. 47, No. SUPPL. 1, pp. 18-22. ISSN: 0378-7346.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Ultrastructure studies of pelvic **peritoneal tissue** from women undergoing laparotomy suggest that before endometriosis has become established in the peritoneum, there might be a metaplastic change by peritoneal mesothelial cells into endometrial glandular cells. A new in vitro experimental model of endometriosis using human ovarian surface

epithelium cells has shown evidence that endometriotic lesions can arise by a process of metaplasia from the ovarian surface epithelium. In this model, when both ovarian surface epithelium and ovarian stromal cells were cocultured with 17beta estradiol in a three-dimensional **collagen** gel lattice, the ovarian surface epithelium cells formed a lumen structure, surrounded by endometrial stromal cells with an epithelial mesenchymal structure. Immunoreactivity for epithelial membrane antigen and cytokeratin was shown in the glandular cells and cilia, as well as in the microvilli. Electron microscopy showed evidence of tight junctions on cell surfaces. These findings suggest that endometriosis may manifest as a serial change from the adjacent mesothelial cells.

L23 ANSWER 5 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:35314 BIOSIS
DOCUMENT NUMBER: PREV199800035314
TITLE: Fibronectin secretion from human **peritoneal tissue** induces Mr 92,000 type IV collagenase expression and invasion in ovarian cancer cell lines.
AUTHOR(S): Shibata, Kiyosumi; Kikkawa, Fumitaka (1); Nawa, Akihiro; Suganuma, Nobuhiko; Hamaguchi, Michinari
CORPORATE SOURCE: (1) Dep. Obstetrics Gynecol., Nagoya Univ. Sch. Med., 65 Tsurumai-cho, Showaku, Nagoya 466 Japan
SOURCE: Cancer Research, (Dec. 1, 1997) Vol. 57, No. 23, pp. 5416-5420.
ISSN: 0008-5472.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Our previous study showed that human peritoneal conditioned medium (CM) increased the matrix metalloproteinase-9 (MMP-9) secretion and invasiveness of ovarian cancer cells (NOM1). In an effort to identify this MMP-9-stimulating factor, we examined the effects of extracellular matrix components, such as type IV **collagen**, laminin, and fibronectin, on ovarian cancer cells. We found that fibronectin increased the MMP-9 activity of NOM1 cell CM in a concentration-dependent manner and that the peritoneal CM contained high level of fibronectin. An increase of MMP-9 activity in NOM1 cell CM by the peritoneal CM was almost completely blocked by 20 mug/ml of anti-integrin alpha5/FnR antibody and RGD polypeptides. Furthermore, after immunoprecipitation by antifibronectin antibody supernatant of the peritoneal CM did not increase MMP-9 activity in NOM1 cells. Fibronectin and the peritoneal CM also increased MMP-9 activity and expression in NOM1 cell lysate, and these effects were blocked by anti-integrin alpha5/FnR antibody. Invasiveness of NOM1 cells was enhanced by fibronectin and the peritoneal CM in a concentration-dependent manner, and anti-integrin alpha5/FnR antibody blocked these effects. These results suggested that fibronectin secreted from peritoneum increased MMP-9 activity and expression, and, in turn, invasiveness of ovarian cancer cells.

IV
laminin
extra cellular matrix components

L23 ANSWER 6 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1997:436221 BIOSIS
DOCUMENT NUMBER: PREV199799735424
TITLE: Ultrastructural study of the peritoneum in patients on continuous ambulatory peritoneal dialysis.
AUTHOR(S): Horita, Yoshio
CORPORATE SOURCE: Second Dep. Pathol., Nagasaki Univ. Sch. Med., Nagasaki Japan
SOURCE: Acta Medica Nagasakiensia, (1997) Vol. 42, No. 1-2, pp. 5-11.
ISSN: 0001-6055.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Twenty peritoneal specimens, collected from 19 patients at the insertion or removal of the catheter for continuous ambulatory peritoneal dialysis (CAPD), were examined by light microscopy (LM) and transmission and scanning electron microscopy (TEM and SEM). During long-term CAPD, the **peritoneal tissue** showed an absence of mesothelial cells and a fibrous thickening by proliferation of degenerative **collagen** fibers. Ultrastructural examination by SEM revealed that the surface of the peritoneum with mesothelial denudation was covered by a continuous

sheet of homogeneous material (a membrane structure) in patients in an the early stage of peritonitis. In cases in the advanced stage, the membrane structure covered the irregular **collagen** bundles, which occasionally showed through breaks in the membrane-like structure. Vascular alterations characterized by the hyalinous degeneration of media, the thickening of the basement membrane in small vasculature, and lymphatic dilatation were observed by TEM in cases of sclerosing peritonitis. Our results suggest that the pathological changes of the peritoneal surface and peripheral blood and lymphatic circulatory impairment may be related to ultrafiltration failure and the progression of pathological process during CAPD.

L23 ANSWER 7 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1988:381667 BIOSIS
DOCUMENT NUMBER: BR35:55595
TITLE: NOVEL BIOMATERIAL OF CROSS-LINKED **PERITONEAL TISSUE**.
AUTHOR(S): LAUREN M D
CORPORATE SOURCE: 160 CANNING STREET, CARLTON, VICTORIA, AUSTRALIA 3053.
PATENT INFORMATION: US 4755593 05 Jul 1988
SOURCE: Off. Gaz. U. S. Pat. Trademark Off., Pat., (1988) 1092 (1), 371.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
FILE SEGMENT: BR; OLD
LANGUAGE: English

L23 ANSWER 8 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1987:208193 BIOSIS
DOCUMENT NUMBER: BA83:105823
TITLE: COAGULOPATHY POST PERITONEOVENOUS SHUNT.
AUTHOR(S): LEVEEN H H; AHMED N; HUTTO R B; IP M; LEVEEN E G
CORPORATE SOURCE: DEP. SURGERY, MED. UNIV. SOUTH CAROLINA, 171 ASHLEY AVE., CHARLESTON, SC 79425.
SOURCE: ANN SURG, (1987) 205 (3), 305-311.
CODEN: ANSUA5. ISSN: 0003-4932.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB In 1942, 53% of medically treated patients with cirrhosis were dead 6 months after the onset of ascites. Only 30% survived 1 year. This dismal outlook has improved only slightly with advances in medicine. Yet, some internists reject the peritoneovenous shunt (PVS) for this fatal condition even if they are aware that a diminished blood volume causes the abnormal sodium retention responsible for ascites. Their objections are based on life-threatening complications of PVS, especially post shunt coagulopathy (PSC). Blood shed into the peritoneal cavity becomes incoagulable. Such blood is immediately coagulated by a protocoagulant (soluble **collagen**) and concurrently lysed by tissue plasminogen activator (TPA) secreted by the peritoneal serosa. Wide zones of lysis surround **peritoneal tissue** placed on fibrin plates. Large volumes of ascitic fluid infused into circulating blood simulates the fate of blood shed into the peritoneal cavity with lysis playing the major role. Addition of ascitic fluid to normal platelet-rich plasma in vitro initiates clot lysis on thromboelastogram (TEG). Epsilon-aminocaproic acid (EACA) counteracts this lysis. EACA and clotting factors normalize the TEG and arrest PSC. Disposal of ascitic fluid at surgery prevents or ameliorates PSC. Mild PSC was encountered only twice in 150+ consecutive patients (1.3%) with only one case being clinically significant (0.6%). Severe PSC occurred seven times in 98 early shunt patients whose ascitic fluid was not discarded. Severe PSC requires shunt interruption and control of bleeding with clotting factors and EACA. Peritoneal lavage with saline prevents the recurrence of PSC on reopening the shunt. In four patients, EACA and clotting factors were adequate to arrest coagulopathy. Three earlier patients died of PSC before its cause and treatment were understood. Proper management eliminates this life-threatening complication, and PSC cannot be considered a deterrent to PVS. Disseminated intravascular coagulopathy (DIC) is produced in experimental animals only by the injection of thrombin or thromboplastin. PSC is a distinct entity differing from DIC; EACA and not heparin is the antidote

for PSC.

L23 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:466687 CAPLUS
TITLE: Dipyridamole inhibits human peritoneal mesothelial cell proliferation in vitro and attenuates rat peritoneal fibrosis in vivo
AUTHOR(S): Hung, Kuan-Yu; Shyu, Ren-Shi; Fang, Cheng-Chung; Tsai, Chien-Chen; Lee, Po-Huang; Tsai, Tun-Jun; Hsieh, Bor-Shen
CORPORATE SOURCE: Departments of Internal Medicine, Emergency Medicine, Surgery, National Taiwan University Hospital, Taipei, Taiwan
SOURCE: Kidney Int. (2001), 59(6), 2316-2324
CODEN: KDYIA5; ISSN: 0085-2538
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background. Peritoneal fibrosis (PF) is one of the most serious complications after long-term continuous ambulatory peritoneal dialysis (CAPD). Proliferation of human peritoneal mesothelial cells (HPMC) and matrix over-prodn. are regarded as the main processes predisposing to PF. Dipyridamole (DP) has been reported to have potential as an antiproliferative and antifibrotic agent. We thus investigated the effect of DP in inhibiting proliferation and **collagen** synthesis of HPMC. A rat model of peritonitis-induced PF was also established to demonstrate the in vivo preventive effect of DP. Methods. HPMC was cultured from human omentum by an enzyme digestion method. Cell proliferation was measured by the methyltetrazolium assay. Intracellular cAMP was measured using an enzyme immunoassay (EIA) kit. Total **collagen** synthesis was measured by 3H-proline incorporation assay. Expression of **collagen** .alpha.1 (I) and **collagen** .alpha.1 (III) mRNAs was detd. by Northern blotting. The rat model of peritonitis-induced PF was developed by adding dextran microbeads (Cytodex, 8 mg/1 mL vol.) to a standardized suspension (3 .times. 109) of Staphylococcus aureus. DP was administrated via i.v. infusion (4 mg in 1 h) daily for seven days. Macroscopic grading of i.p. adhesions and histol. analyses of peritoneal thickness and **collagen** expression were performed. Results. Addn. of DP to HPMC cultures suppressed serum-stimulated cell proliferation and **collagen** synthesis. The antimitogenic and antifibrotic effects of DP appear to be predominantly mediated through the cAMP pathway, as DP increased intracellular cAMP in a dose-dependent manner. The macroscopic grade of i.p. adhesion and peritoneal thickness were both significantly increased in animals treated with Cytodex plus S. aureus; on the other hand, DP attenuated these fibrotic changes with statistical significance ($P < 0.01$). Anal. of gene expression of **collagen** .alpha.1 (I) and .alpha.1 (III) in the **peritoneal tissue** of exptl. animals yielded similar results. Conclusions. This study suggests that dipyridamole may have therapeutic potential in treating peritoneal fibrosis.
REFERENCE COUNT: 23
REFERENCE(S): (4) Fang, C; Kidney Int 2000, V57, P2626 CAPLUS
(5) Fang, C; Nephrol Dial Transplant 1996, V11, P2276 CAPLUS
(8) Fracasso, A; Am J Kidney Dis 1999, V33, P105 CAPLUS
(10) Hillis, G; Nephron 1998, V78, P172 CAPLUS
(12) Iimura, O; Eur J Pharmacol 1996, V296, P319 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:414934 CAPLUS
DOCUMENT NUMBER: 133:294843
TITLE: Expression of heat shock proteins 47 and 70 in the peritoneum of patients on continuous ambulatory peritoneal dialysis
AUTHOR(S): Shioshita, Kei; Miyazaki, Masanobu; Ozono, Yoshiyuki; Abe, Katsushige; Taura, Kouichi; Harada, Takashi;

CORPORATE SOURCE: Koji, Takehiko; Taguchi, Takashi; Kohno, Shigeru
The Second Department of Internal Medicine, Division of Renal Care Unit, Department of Histology and Cell Biology, Nagasaki University School of Medicine, Nagasaki, Japan

SOURCE: Kidney Int. (2000), 57(2), 619-631
CODEN: KDYIA5; ISSN: 0085-2538
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background. Peritoneal sclerosis, characterized by **collagen** accumulation, is a serious complication in continuous ambulatory peritoneal dialysis (CAPD) therapy. Heat shock protein 47 (HSP47) is a **collagen**-specific mol. chaperon and is closely assocd. with **collagen** synthesis. Methods. We detd. the expression of HSP47 and HSP70 (nonspecific for **collagen** synthesis) by immunohistochem. in **peritoneal tissues** of patients on CAPD. The tissue for **collagen** III, .alpha.-smooth muscle actin (.alpha.-SMA), and CD68 (a marker for macrophages) were also stained. Thirty-two peritoneal samples were divided into three groups (group A1, 11 patients who had no ultrafiltration loss; group A2, 9 patients who had ultrafiltration loss; and group B, 12 specimens who had endstage renal disease prior to induction of CAPD). Results. In group B, staining for HSP47, HSP70, and **collagen** III in **peritoneal tissues** was faint, and only a few cells were pos. for .alpha.-SMA and CD68. In contrast, HSP47, HSP70, and **collagen** III were expressed in areas of thickened connective tissues in fibrotic peritoneal specimens of CAPD patients. The expression level of HSP47, HSP70, **collagen** III, and .alpha.-SMA and the no. of CD68-pos. cells in group A2 were significantly higher than those in group A1 and B. HSP47/HSP70-pos. cells were mesothelial cells, adipocytes, and .alpha.-SMA-pos. myofibroblasts. Furthermore, the expression level of HSP47 was significantly higher in peritoneal specimens from patients with refractory peritonitis than without it and was significantly higher in patients with more than 60 mo of CAPD therapy than that in patients with less than 60 mo of CAPD. Conclusion. Our results indicate that CAPD therapy may induce HSPs in the **peritoneal tissue**, and that peritonitis in CAPD patients may be assocd. with the progression of peritoneal sclerosis at least through HSP47 expression and chronic macrophage infiltration. Our data also suggest that the progression of peritoneal sclerosis in such patients is assocd. with deterioration of peritoneal ultrafiltration function.

REFERENCE COUNT: 36
REFERENCE(S):
(3) Cheng, M; Int J Exp Pathol 1998, V79, P125 CAPLUS
(4) Cryer, A; Eur J Clin Invest 1982, V12, P235 CAPLUS
(5) Darby, I; Lab Invest 1990, V63, P21 CAPLUS
(6) Desmouliere, A; J Cell Biol 1993, V122, P103 CAPLUS
(11) Heydari, A; Dev Genet 1996, V18, P114 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 11 OF 18 CAPLUS

ACCESSION NUMBER: 1997:775913 CAPLUS
DOCUMENT NUMBER: 128:60104

TITLE: Fibronectin secretion from human **peritoneal tissue** induces Mr 92,000 type IV collagenase expression and invasion in ovarian cancer cell lines

AUTHOR(S): Shibata, Kiyosumi; Kikkawa, Fumitaka; Nawa, Akihiro; Suganuma, Nobuhiko; Hamaguchi, Michinari

CORPORATE SOURCE: Departments of Obstetrics and Gynecology, Nagoya University School of Medicine, Nagoya, 466, Japan

SOURCE: Cancer Res. (1997), 57(23), 5416-5420
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The previous study showed that human peritoneal conditioned medium (CM) increased the matrix metalloproteinase-9 (MMP-9) secretion and invasiveness of ovarian cancer cells (NOM1). In an effort to identify this MMP-9-stimulating factor, the authors examd. the effects of

extracellular matrix components, such as type IV **collagen**, laminin, and fibronectin, on ovarian cancer cells. The authors found that fibronectin increased the MMP-9 activity of NOM1 cell CM in a concn.-dependent manner and that the peritoneal CM contained high level of fibronectin. An increase of MMP-9 activity in NOM1 cell CM by the peritoneal CM was almost completely blocked by 20 .mu.g/mL of anti-integrin .alpha.5/FnR antibody and RGD polypeptides. Furthermore, after immunopptn. by antifibronectin antibody supernatant of the peritoneal CM did not increase MMP-9 activity in NOM1 cells. Fibronectin and the peritoneal CM also increased MMP-9 activity and expression in NOM1 cell lysate, and these effects were blocked by anti-integrin .alpha.5/FnR antibody. Invasiveness of NOM1 cells was enhanced by fibronectin and the peritoneal CM in a concn.-dependent manner, and anti-integrin .alpha.5/FnR antibody blocked these effects. These results suggested that fibronectin secreted from peritoneum increased MMP-9 activity and expression, and, in turn, invasiveness of ovarian cancer cells.

L23 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1988:535012 CAPLUS
DOCUMENT NUMBER: 109:135012
TITLE: Crosslinked **peritoneal tissues** as novel biomaterials for medical devices and process for their manufacture
INVENTOR(S): Lauren, Mark D.
PATENT ASSIGNEE(S): Australia
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4755593	A	19880705	US 1986-888717	19860724
AU 8660596	A1	19870129	AU 1986-60596	19850724

PRIORITY APPLN. INFO.: AU 1985-1616 19850724
AB A biomaterial, suitable for use in medical devices, comprises peritoneum tissue which has been chem. treated to crosslink the **collagen** in the tissue, rendering the tissue more stable, less antigenic, and sterile. Peritoneum tissue was dissected from the abdominal cavity of calves, the tissue cleaned in phosphate buffered saline, pinned to a polyethylene surface, and exposed to 1% glutaraldehyde in phosphate buffered saline for 24 h at room temp., followed by 2% H2O2 for 30 min, and stored in 50% aq. EtOH. The treated tissue had shrinkage temp. 83.5.degree., vs. 66.5 and 67.5.degree. for untreated tissue.

L23 ANSWER 13 OF 18 MEDLINE
ACCESSION NUMBER: 2001296011 MEDLINE
DOCUMENT NUMBER: 21275842 PubMed ID: 11380836
TITLE: Dipyridamole inhibits human peritoneal mesothelial cell proliferation in vitro and attenuates rat peritoneal fibrosis in vivo.
AUTHOR: Hung K Y; Shyu R S; Fang C C; Tsai C C; Lee P H; Tsai T J; Hsieh B S
CORPORATE SOURCE: Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, Republic of China.
SOURCE: KIDNEY INTERNATIONAL, (2001 Jun) 59 (6) 2316-24.
Journal code: KVB; 0323470. ISSN: 0085-2538.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20010813
Entered Medline: 20010809
AB BACKGROUND: Peritoneal fibrosis (PF) is one of the most serious complications after long-term continuous ambulatory peritoneal dialysis

(CAPD). Proliferation of human peritoneal mesothelial cells (HPMC) and matrix over-production are regarded as the main processes predisposing to PF. Dipyridamole (DP) has been reported to have potential as an antiproliferative and antifibrotic agent. We thus investigated the effect of DP in inhibiting proliferation and **collagen** synthesis of HPMC. A rat model of peritonitis-induced PF was also established to demonstrate the in vivo preventive effect of DP. METHODS: HPMC was cultured from human omentum by an enzyme digestion METHOD: Cell proliferation was measured by the methyltetrazolium assay. Intracellular cAMP was measured using an enzyme immunoassay (EIA) kit. Total **collagen** synthesis was measured by (3)H-proline incorporation assay. Expression of **collagen** alpha1 (I) and **collagen** alpha 1 (III) mRNAs was determined by Northern blotting. The rat model of peritonitis-induced PF was developed by adding dextran microbeads (Cytodex, 8 mg/1 mL volume) to a standardized suspension (3 x 10(9)) of Staphylococcus aureus. DP was administrated via intravenous infusion (4 mg in 1 h) daily for seven days. Macroscopic grading of intraperitoneal adhesions and histological analyses of peritoneal thickness and **collagen** expression were performed. RESULTS: Addition of DP to HPMC cultures suppressed serum-stimulated cell proliferation and **collagen** synthesis. The antimitogenic and antifibrotic effects of DP appear to be predominantly mediated through the cAMP pathway, as DP increased intracellular cAMP in a dose-dependent manner. The macroscopic grade of intraperitoneal adhesion and peritoneal thickness were both significantly increased in animals treated with Cytodex plus S. aureus; on the other hand, DP attenuated these fibrotic changes with statistical significance ($P < 0.01$). Analysis of gene expression of **collagen** alpha 1 (I) and alpha1 (III) in the **peritoneal tissue** of experimental animals yielded similar results. CONCLUSIONS: This study suggests that dipyridamole may have therapeutic potential in treating peritoneal fibrosis.

L23 ANSWER 14 OF 18 MEDLINE

ACCESSION NUMBER: 2000117971 MEDLINE
DOCUMENT NUMBER: 20117971 PubMed ID: 10652040
TITLE: Expression of heat shock proteins 47 and 70 in the peritoneum of patients on continuous ambulatory peritoneal dialysis.
AUTHOR: Shioshita K; Miyazaki M; Ozono Y; Abe K; Taura K; Harada T; Koji T; Taguchi T; Kohno S
CORPORATE SOURCE: The Second Department of Internal Medicine, Nagasaki University School of Medicine, Sakamoto, Japan.
SOURCE: KIDNEY INTERNATIONAL, (2000 Feb) 57 (2) 619-31. Journal code: KVB; 0323470. ISSN: 0085-2538.
PUB. COUNTRY: United States
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: English
ENTRY MONTH: Priority Journals
ENTRY DATE: 200003
Entered STN: 20000320
Last Updated on STN: 20000320
Entered Medline: 20000309

AB BACKGROUND: Peritoneal sclerosis, characterized by **collagen** accumulation, is a serious complication in continuous ambulatory peritoneal dialysis (CAPD) therapy. Heat shock protein 47 (HSP47) is a **collagen**-specific molecular chaperon and is closely associated with **collagen** synthesis. METHODS: We determined the expression of HSP47 and HSP70 (nonspecific for **collagen** synthesis) by immunohistochemistry in **peritoneal tissues** of patients on CAPD. The tissue for **collagen** III, alpha-smooth muscle actin (alpha-SMA), and CD68 (a marker for macrophages) were also stained. Thirty-two peritoneal samples were divided into three groups (group A1, 11 patients who had no ultrafiltration loss; group A2, 9 patients who had ultrafiltration loss; and group B, 12 specimens who had end-stage renal disease prior to induction of CAPD. RESULTS: In group B, staining for HSP47, HSP70, and **collagen** III in **peritoneal tissues** was faint, and only a few cells were positive for alpha-SMA and CD68. In contrast, HSP47, HSP70, and **collagen** III were expressed in areas of thickened connective tissues in fibrotic

peritoneal specimens of CAPD patients. The expression level of HSP47, HSP70, **collagen** III, and alpha-SMA and the number of CD68-positive cells in group A2 were significantly higher than those in groups A1 and B. HSP47/HSP70-positive cells were mesothelial cells, adipocytes, and alpha-SMA-positive myofibroblasts. Furthermore, the expression level of HSP47 was significantly higher in peritoneal specimens from patients with refractory peritonitis than without it and was significantly higher in patients with more than 60 months of CAPD therapy than that in patients with less than 60 months of CAPD. CONCLUSION: Our results indicate that CAPD therapy may induce HSPs in the **peritoneal tissue**, and that peritonitis in CAPD patients may be associated with the progression of peritoneal sclerosis at least through HSP47 expression and chronic macrophage infiltration. Our data also suggest that the progression of peritoneal sclerosis in such patients is associated with deterioration of peritoneal ultrafiltration function.

L23 ANSWER 15 OF 18 MEDLINE
ACCESSION NUMBER: 1999189202 MEDLINE
DOCUMENT NUMBER: 99189202 PubMed ID: 10087424
TITLE: Coelomic metaplasia theory of endometriosis: evidence from in vivo studies and an in vitro experimental model.
AUTHOR: Matsuura K; Ohtake H; Katabuchi H; Okamura H
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Kumamoto University School of Medicine, Kumamoto, Japan.
SOURCE: GYNECOLOGIC AND OBSTETRIC INVESTIGATION, (1999) 47 Suppl 1 18-20; discussion 20-2.
Journal code: FYA; 7900587. ISSN: 0378-7346.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990730
Last Updated on STN: 19990730
Entered Medline: 19990722
AB Ultrastructure studies of pelvic **peritoneal tissue** from women undergoing laparotomy suggest that before endometriosis has become established in the peritoneum, there might be a metaplastic change by peritoneal mesothelial cells into endometrial glandular cells. A new in vitro experimental model of endometriosis using human ovarian surface epithelium cells has shown evidence that endometriotic lesions can arise by a process of metaplasia from the ovarian surface epithelium. In this model, when both ovarian surface epithelium and ovarian stromal cells were cocultured with 17beta estradiol in a three-dimensional **collagen** gel lattice, the ovarian surface epithelium cells formed a lumen structure, surrounded by endometrial stromal cells with an epithelial mesenchymal structure. Immunoreactivity for epithelial membrane antigen and cytokeratin was shown in the glandular cells and cilia, as well as in the microvilli. Electron microscopy showed evidence of tight junctions on cell surfaces. These findings suggest that endometriosis may manifest as a serial change from the adjacent mesothelial cells.

L23 ANSWER 16 OF 18 MEDLINE
ACCESSION NUMBER: 1998053918 MEDLINE
DOCUMENT NUMBER: 98053918 PubMed ID: 9393769
TITLE: Fibronectin secretion from human **peritoneal tissue** induces Mr 92,000 type IV collagenase expression and invasion in ovarian cancer cell lines.
AUTHOR: Shibata K; Kikkawa F; Nawa A; Suganuma N; Hamaguchi M
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Nagoya University School of Medicine, Japan.
SOURCE: CANCER RESEARCH, (1997 Dec 1) 57 (23) 5416-20.
Journal code: CNF; 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980312

Last Updated on STN: 20000303
Entered Medline: 19980302

AB Our previous study showed that human peritoneal conditioned medium (CM) increased the matrix metalloproteinase-9 (MMP-9) secretion and invasiveness of ovarian cancer cells (NOM1). In an effort to identify this MMP-9-stimulating factor, we examined the effects of extracellular matrix components, such as type IV **collagen**, laminin, and fibronectin, on ovarian cancer cells. We found that fibronectin increased the MMP-9 activity of NOM1 cell CM in a concentration-dependent manner and that the peritoneal CM contained high level of fibronectin. An increase of MMP-9 activity in NOM1 cell CM by the peritoneal CM was almost completely blocked by 20 microg/ml of anti-integrin alpha5/FnR antibody and RGD polypeptides. Furthermore, after immunoprecipitation by antifibronectin antibody supernatant of the peritoneal CM did not increase MMP-9 activity in NOM1 cells. Fibronectin and the peritoneal CM also increased MMP-9 activity and expression in NOM1 cell lysate, and these effects were blocked by anti-integrin alpha5/FnR antibody. Invasiveness of NOM1 cells was enhanced by fibronectin and the peritoneal CM in a concentration-dependent manner, and anti-integrin alpha5/FnR antibody blocked these effects. These results suggested that fibronectin secreted from peritoneum increased MMP-9 activity and expression, and, in turn, invasiveness of ovarian cancer cells.

L23 ANSWER 17 OF 18 MEDLINE
ACCESSION NUMBER: 91120610 MEDLINE
DOCUMENT NUMBER: 91120610 PubMed ID: 2487245
TITLE: Mitogenic and protein synthetic activity of tissue repair cells: control by the postsurgical macrophage.
AUTHOR: Fukasawa M; Campeau J D; Yanagihara D L; Rodgers K E; Dizerega G S
CORPORATE SOURCE: Department of Obstetrics and Gynecology, University of Southern California School of Medicine, Los Angeles 90033.
CONTRACT NUMBER: NICHD 19001 (NICHD)
SOURCE: JOURNAL OF INVESTIGATIVE SURGERY, (1989) 2 (2) 169-80.
Journal code: AZA; 8809255. ISSN: 0894-1939.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199103
ENTRY DATE: Entered STN: 19910405
Last Updated on STN: 19910405
Entered Medline: 19910314

AB It is well known that fibroblasts are a main source of extracellular matrix synthesis necessary for tissue repair. In addition, macrophages secrete products that are known to modulate synthesis of extracellular matrix. Accordingly, we studied the incorporation of [3H]thymidine, [3H]proline, and [35S]sulfate into macromolecules produced by fibroblasts recovered from the site of **peritoneal tissue** repair cultured with and without spent media from postsurgical peritoneal macrophages. Rabbits underwent resection and reanastomosis of their small intestines. Peritoneal exudative cells (PEC) were then collected on postsurgical day 5 and day 10 as well as from nonsurgical controls, separated by discontinuous Percoll gradient centrifugation, and cultured for 48 h. A second group of rabbits underwent peritoneal wall abrasion from which fibroblast tissue repair cells (TRC) were collected from the site of injury at postsurgical day 7 and maintained in culture for varying times. Incorporation of radiolabeled precursors into DNA, **collagen**, and sulfated proteoglycans was determined. Incorporation of [3H]thymidine and [3H]proline into untreated TRC gradually decreased with culture duration. Conversely, [35S]sulfate incorporation gradually increased during prolonged culture. Macrophage spent media increased the levels of [3H]thymidine incorporation by the TRC. [3H]Proline and [35S]sulfate incorporation into TRC were also stimulated by macrophage spent media. However, this stimulation may be due to the enhanced proliferation of TRC by macrophage spent media. In conclusion, tissue repair fibroblasts are activated for postsurgical repair at the site of injury by many factors including secretory products from postsurgical macrophages.

L23 ANSWER 18 OF 18 MEDLINE
ACCESSION NUMBER: 87155540 MEDLINE
DOCUMENT NUMBER: 87155540 PubMed ID: 3103556
TITLE: Coagulopathy post peritoneovenous shunt.
AUTHOR: LeVeen H H; Ip M; Ahmed N; Hutto R B; LeVeen E G
SOURCE: ANNALS OF SURGERY, (1987 Mar) 205 (3) 305-11.
Journal code: 67S; 0372354. ISSN: 0003-4932.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198704
ENTRY DATE: Entered STN: 19900303
Last Updated on STN: 19980206
Entered Medline: 19870403

AB In 1942, 53% of medically treated patients with cirrhosis were dead 6 months after the onset of ascites. Only 30% survived 1 year. This dismal outlook has improved only slightly with advances in medicine. Yet, some internists reject the peritoneovenous shunt (PVS) for this fatal condition even if they are aware that a diminished blood volume causes the abnormal sodium retention responsible for ascites. Their objections are based on life-threatening complications of PVS, especially post shunt coagulopathy (PSC). Blood shed into the peritoneal cavity becomes incoagulable. Such blood is immediately coagulated by a protocoagulant (soluble **collagen**) and concurrently lysed by tissue plasminogen activator (TPA) secreted by the peritoneal serosa. Wide zones of lysis surround **peritoneal tissue** placed on fibrin plates. Large volumes of ascitic fluid infused into circulating blood simulates the fate of blood shed into the peritoneal cavity with lysis playing the major role. Addition of ascitic fluid to normal platelet-rich plasma in vitro initiates clot lysis on thromboelastogram (TEG). Epsilon-aminocaproic acid (EACA) counteracts this lysis. EACA and clotting factors normalize the TEG and arrest PSC. Disposal of ascitic fluid at surgery prevents or ameliorates PSC. Mild PSC was encountered only twice in 150+ consecutive patients (1.3%) with only one case being clinically significant (0.6%). Severe PSC occurred seven times in 98 early shunt patients whose ascitic fluid was not discarded. Severe PSC requires shunt interruption and control of bleeding with clotting factors and EACA. Peritoneal lavage with saline prevents the recurrence of PSC on reopening the shunt. In four patients, EACA and clotting factors were adequate to arrest coagulopathy. Three earlier patients died of PSC before its cause and treatment were understood. Proper management eliminates this life-threatening complication, and PSC cannot be considered a deterrent to PVS. Disseminated intravascular coagulopathy (DIC) is produced in experimental animals only by the injection of thrombin or thromboplastin. PSC is a distinct entity differing from DIC; EACA and not heparin is the antidote for PSC.

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(FILE 'HOME' ENTERED AT 15:17:07 ON 10 DEC 2001)

FILE 'BIOSIS, CAPLUS, MEDLINE' ENTERED AT 15:17:53 ON 10 DEC 2001

L1	92198	S	IMPLANTS
L2	233782	S	COLLAGEN
L3	15971	S	NERVE (W) REGENERATION
L4	3929	S	L1 AND L2
L5	69	S	L4 AND L3
L6	18290	S	TYPE (W) I (W) COLLAGEN
L7	5051	S	TYPE (W) III (W) COLLAGEN
L8	11105	S	TYPE (W) IV (W) COLLAGEN
L9	8	S	L5 AND L6
L10	0	S	L5 AND L7
L11	0	S	L5 AND L8
L12	2183	S	L7 AND L6
L13	1542	S	L8 AND L6
L14	3	S	L3 AND L12

L15	3	S	L3 AND L13
L16	41664	S	NERVE GROWTH FACTOR
L17	5	S	L16 AND L5
L18	33671	S	LAMININ
L19	18	S	L18 AND L5
L20	387	S	PERITONEAL TISSUE
L21	0	S	L20 AND L5
L22	0	S	L20 AND L3
L23	18	S	L20 AND L2
L24	0	S	L20 AND L4